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Title of Invention: _____

Inventors (please provide full names): JUALANG HWANG; CHIA-TSE HSU; CHUN-JEN TING

Earliest Priority Date: 10-05-99

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Devi, S.
09/412558

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S1 1289 PSEUDOMONAS(10N)((EXOTOXIN OR EXO(W)TOXIN)(W)A)
S2 904 S1 AND (PEPTIDE? ? OR PROTEIN? ? OR POLYPEPTIDE? ? OR POLY-PROTEIN? ? OR GNRH? ? OR (GN OR GONADOTROP?)(W)(RH OR RELEAS?-(W)HORMONE? ?))
S3 30 S2 AND RECEPTOR(W)BINDING(W)DOMAIN? ?
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8/3,AB/1 (Item 1 from file: 35)
DIALOG(R)File 35:Dissertation Abs Online
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01413901 AADAAI9517013
STRUCTURE-FUNCTION STUDIES OF *PSEUDOMONAS"** AERUGINOSA *EXOTOXIN"** *A"**
Author: HAN, XIANG-YANG
Degree: PH.D.
Year: 1994
Corporate Source/Institution: THE OHIO STATE UNIVERSITY (0168)
Source: VOLUME 56/01-B OF DISSERTATION ABSTRACTS INTERNATIONAL.
PAGE 63. 142 PAGES

Pseudomonas aeruginosa is a bacterium which frequently causes infections in immunocompromised individuals. P. aeruginosa produces a number of virulence factors, one of which is exotoxin A. Exotoxin A is a 66-kDa *protein"** toxin which is cytotoxic for target eukaryotic cells due to its ADP-ribosylation activity. Using NAD$\sp+$ as the ADP-ribose donor,

exotoxin A enzymatically catalyzes the ADP-ribosylation of elongation factor-2 (EF-2), resulting in the inactivation of this *protein"** factor which is required for cellular *protein"** synthesis. Exotoxin A has three domains: the enzymatic domain (residues 405 to 613), the *receptor"** *binding"** *domain"** (residues 1 to 252, 364 to 404) and the membrane translocation domain (residues 253 to 363).

The present study analyzed the function of two key histidine residues, His-426 and His-440, located in the enzymatic domain, using site-directed mutagenesis to produce substitutions at these sites. The role of His-426 was studied by analyzing mutant toxins with Tyr-426 and Leu-426 substitutions. Both substitutions reduce ADP-ribosylation activity 10- to 30-fold. These substitutions also result in significant thermal instability of the altered toxins. Binding of a conformation-sensitive monoclonal antibody was abolished or reduced following substitutions at this site, implying that His-426 is a key residue within the conformation-dependent epitope. These results, along with location of the residue within the three-dimensional structure of exotoxin A, suggest that His-426 participates in maintaining thermal stability of the toxin. Based on these studies, it is proposed that when toxin is in the active configuration, His-426 stabilizes the active conformation required for the efficient binding of the EF-2 substrate.

The role of His-440 was explored by analyzing Ala, Phe and Asn substitutions at this site. These substitutions diminish ADP-ribosylation activity greater than 1000-fold. The ability to inhibit eukaryotic *protein"** synthesis in mouse fibroblastoid L-929 cells is also significantly reduced. NAD$\sp+$ binding appears to be unaffected as a result of these substitutions, as indicated by similar K$\sb{\rm m}$ values. These results, together with crystallographic findings indicating that His-440 is located within or close to the proposed NAD$\sp+$ binding site, suggest that His-440 is a catalytic residue involved in the transfer of the ADP-ribose moiety onto the EF-2 substrate.

NAD$\sp+$ analogues were also studied for possible substrate activity as ADP-ribose donors for exotoxin A. Results show that NADH and thio-NAD$\sp+$ can be used as ADP-ribose donors resulting in the covalent modification of EF-2. The velocity of this reaction using NADH is approximately one fifth the rate observed with NAD$\sp+$. Due to the coexistence of NAD$\sp+$ and NADH within the cell, the substrate activity of NADH could possibly be of pathogenic significance during cytotoxic events associated with the uptake of exotoxin A.

01308463 AAD9324742
MOLECULAR STUDIES ON THE ENVIRONMENTAL FACTORS THAT REGULATE *EXOTOXIN"** *A"** PRODUCTION IN *PSEUDOMONAS"** AERUGINOSA
Author: PRINCE, ROBERT WILLIAM
Degree: PH.D.
Year: 1993
Corporate Source/Institution: UNIVERSITY OF COLORADO HEALTH SCIENCES CENTER (0831)
Source: VOLUME 54/04-B OF DISSERTATION ABSTRACTS INTERNATIONAL. PAGE 1786. 121 PAGES

Evidence of presented in this thesis that the E. coli fur gene can affect the regulation of toxA and regAB when present in *multiple"**

*copies"** in Pseudomonas aeruginosa strain PA103C. PA103C contains a toxA::lacZ fusion integrated into its chromosome at the toxA locus. β-galactosidase synthesis and exotoxin A production in PA103C containing *multiple"** *copies"** of E. coli fur was repressed in both high- and low-iron media. In addition, stead-state levels of the T1 transcript produced from the regAB operon was reduced in strain PA103C which contained *multiple"** *copies"** of E. coli fur.

A polyclonal rabbit serum containing antibodies that recognize E. coli Fur was used to screen whole-cell extracts from Pseudomonas aeruginosa. A *protein"** that was specifically recognized by the anti-Fur serum was identified. This cross-reactive Fur *protein"** was purified from strain PA103 and a partial amino-terminal sequence was obtained. This sequence was found to be homologous with the amino-terminal sequence of E. coli Fur.

These data suggested that a Fur homologue existed in P. aeruginosa; therefore, an attempt was made to clone this gene from P. aeruginosa. A 5.9 Kb DNA fragment was cloned from P. aeruginosa strain PA103 that could complement the Fur$\sp{-}$ phenotype of an E. coli fur mutant. Sequencing of the 5.9 Kb DNA fragment identified an open reading frame predicted to encode a *protein"** 50% identical to E. coli Fur and 48% identical to V. cholerae Fur.

These studies also describe a selection procedure that was used to isolate manganese resistant mutants of strain PA103, some of which produce altered Fur *proteins"**. These manganese resistant Fur mutants constitutively produce siderophores and exotoxin A in concentrations of iron ($>$10 μM) that normally repress their production. When a multicopy plasmid carrying the P. aeruginosa fur gene is introduced into one of these Fur mutant PA103 strains, manganese susceptibility and wild type regulation of exotoxin A and siderophore production is restored.

In addition, studies are presented which suggested that toxA is regulated by the P. aeruginosa anr gene.

8/3,AB/3 (Item 3 from file: 35)
DIALOG(R)File 35:Dissertation Abs Online

01178236 AAD9130519
*PSEUDOMONAS"** AERUGINOSA *EXOTOXIN"** *A"**: IMMUNOCHEMICAL ANALYSIS OF THE PROPOSED ELONGATION FACTOR 2 BINDING SITE AND ADP-RIBOSYLTRANSFERASE CROSS-REACTIVE EPITOPE
Author: MCGOWAN, JEAN LOUISE
Degree: PH.D.
Year: 1991
Corporate Source/Institution: THE OHIO STATE UNIVERSITY (0168)
Source: VOLUME 52/05-B OF DISSERTATION ABSTRACTS INTERNATIONAL.
PAGE 2413. 113 PAGES

The opportunistic pathogen Pseudomonas aeruginosa is the causative agent of nosocomial infections and the extracellular *protein"** exotoxin A (ETA) is a primary virulence factor. ETA is a member of a class of bacterial ADP-ribosyltransferases that includes diphtheria, cholera and pertussis toxins. These toxins catalyze the covalent attachment of the ADP-ribose moiety of NAD$\sp+$ to a mammalian target *protein"**. Exotoxin A inhibits *protein"** synthesis through the covalent modification of elongation factor 2 (EF-2).

ETA has three structural domains. Domain I at the amino-terminus is involved in cell *receptor"** *binding"**. *Domain"** II is a proposed translocation domain, and domain III contains the catalytic activity. A

mutant toxin (CRM-66) has been isolated that lacks ADPRT activity. The inability of CRM-66 to ADP-ribosylate EF-2 results from a histidine to tyrosine substitution at position 426 (Y426H).

A combined approach using monoclonal antibodies and synthetic *peptides"** has revealed that the binding site on toxin for EF-2 is hidden in the proenzyme conformation and becomes exposed followed activation. Mab TC-1 does not recognize CRM-66 and inhibits the ADPRT activity of ETA. The epitope of TC-1 was defined as the sequence 422-432 which is in a helical segment. Site-specific antisera against *peptide"** 419-432 inhibits the ADPRT activity of ETA, but does not affect the NAD$\sp+$ glycohydrolase activity. This suggests that TC-1 and the *peptide"** antibody are interfering with the interaction of ETA and its *protein"** substrate EF-2. Additionally, we propose that activation of ETA results in a conformational change that exposes His 426 and allows EF-2 to bind.

Several Mabs prepared against ETA cross-react with diphtheria, cholera and pertussis toxins. Some of these Mabs (T20) inhibit the ADPRT activity of ETA but do not inhibit glycohydrolase activity. The epitope of T20 was analyzed using synthetic *peptides"** and resides within the sequence 419-432. Antibody against 419-432 and 427-438 recognize diphtheria, cholera, and pertussis toxins, as well as ETA. Additionally, these antibodies inhibit the ADPRT of ETA and diphtheria toxin. Binding of anti-diphtheria antibody to diphtheria is blocked by *peptides"** 419-432 and 427-438. These data suggest the existance of a homologous sequence within the ADPRT toxins.

8/3,AB/4 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

14770224 PASCAL No.: 00-0449348

Vaccination against *gonadotropin"**-*releasing"** *hormone"** (*GnRH"**) using toxin *receptor"**-*binding"** *domain"**-conjugated *GnRH"** *repeats"**

HSU C T; TING C Y; TING C J; CHEN T Y; LIN C P; WHANG-PENG J; JAULANG HWANG

Graduate Institute of Life Science, National Defense Medical Center, Academia Sinica, Taipei, 11529, Taiwan; Institute of Molecular Biology, Academia Sinica, Taipei, 11529, Taiwan; Division of Drug Biology, National Laboratories of Foods and Drugs, Department of Health, Taipei, Taiwan

Journal: Cancer research : (Baltimore), 2000, 60 (14) 3701-3705

Language: English

A method for the preparation of an immunogen containing *multiple"** *copies"** of a self-*peptide"** in linear alignment was designed in order to overcome the difficulty of inducing an immune response to poorly immunogenic *peptide"** antigens. DNA fragments encoding multiple *repeats"** of the self-*peptide"** were generated by a new technique, termed template-*repeated"** polymerase chain reaction (TR-PCR), which could be subcloned into an expression vector for production of *peptide"** *repeats"** as an immunogen. This approach was tested by constructing fusion *proteins"** containing the *receptor"**-*binding"** *domain"** of *Pseudomonas"** *exotoxin"** *A"** and *multiple"** *copies"** of the 10-residue sequence of the *peptide"** hormone *gonadotropin"**-*releasing"** *hormone"** (*GnRH"**). Immunization of female rabbits with the immunogen that contained the exotoxin *receptor"**-*binding"** *domain"** and 12 *copies"** of *GnRH"** (PEIa-*GnRH"** SUB 1 SUB 2) resulted in the generation of high-titer antibodies specific for *GnRH"**. Although at equal molar basis of the *GnRH"** moiety, the immunogen that

contained single copy of *GnRH"** (PEIa-*GnRH"** SUB 1) induced low-titer anti-*GnRH"** antibodies. These observations suggest that the presence of multiple *peptide"** *repeats"** is a key factor in eliciting an immune response. In addition, anti-*GnRH"** antibodies effectively neutralized *GnRH"** activity in vivo, as demonstrated by the degeneration of the ovaries in the injected rabbits. Because anti-*GnRH"** antibody could be functionally analogous to *GnRH"** antagonist, which has been used to treat patients with ovarian cancer, vaccination of PEIa-*GnRH"** SUB 1 SUB 2 presents a potential therapeutic application for the treatment of *GnRH"** -sensitive ovarian cancer.

8/3,AB/5 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

11028330 PASCAL No.: 93-0537836
Coordinate regulation of siderophore and *exotoxin"** *A"** production : molecular cloning and sequencing of the *Pseudomonas"** aeruginosa fur gene
PRINCE R W; COX C D; VASIL M L
Univ. Colorado health sci. cent., dep. microbiology/immunology B-175, Denver CO 80262, USA
Journal: Journal of bacteriology, 1993, 175 (9) 2589-2598
Language: English
A 5.9-kb DNA fragment was cloned from Pseudomonas aeruginosa PA103 by its ability to functionally complement a fur mutation in Escherichia coli. A fur null mutant E. coli strain that contains *multiple"** *copies"** of the 5.9-kb DNA fragment produces a 15-kDa *protein"** which cross-reacts with a polyclonal anti-E. coli Fur serum. Sequencing of a subclone of the 5.9-kb DNA fragment identified an open reading frame predicted to encode a *protein"** 53% identical to E. coli Fur and 49% identical to Vibrio cholerae Fur and Yersinia pestis Fur. While there is extensive homology among these Fur *proteins"**, Fur from P. aeruginosa differs markedly at its carboxy terminus from all of the other Fur *proteins"**

8/3,AB/6 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

13163465 GENUINE ARTICLE#: 485DX NUMBER OF REFERENCES: 54
TITLE: Dual-function vaccine for *Pseudomonas"** aeruginosa:
Characterization of chimeric *exotoxin"** *A"**-pilin *protein"**
AUTHOR(S): Hertle R; Mrsny R; Fitzgerald DJ (REPRINT)
AUTHOR(S) E-MAIL: djpf@helix.nih.gov
CORPORATE SOURCE: NCI, CCR, Bldg 37,4B03,37 Convent Dr,MSC 4255/Bethesda//MD/20892 (REPRINT); NCI, CCR, /Bethesda//MD/20892; Genentech Inc, /S San Francisco//CA/94080
PUBLICATION TYPE: JOURNAL
PUBLICATION: INFECTION AND IMMUNITY, 2001, V69, N11 (NOV), P6962-6969
PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA
ISSN: 0019-9567
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: Pseudomonas aeruginosa is the major infectious agent of concern for cystic fibrosis patients. Strategies to prevent colonization by

this bacterium and/or neutralize its virulence factors are clearly needed. Here we characterize a dual-function vaccine designed to generate antibodies to reduce bacterial adherence and to neutralize the cytotoxic activity of exotoxin A. To construct the vaccine, key sequences from type IV pilin were inserted into a vector encoding a nontoxic (active-site deletion) version of exotoxin A. The chimeric *protein"**, termed PE64 Delta 553pil, was expressed in Escherichia coli, refolded to a near-native conformation, and then characterized by various biochemical and immunological assays. PE64 Delta 553pil bound specifically to asialo-GM1, and, when injected into rabbits, produced antibodies that reduced bacterial adherence and neutralized the cell-killing activity of exotoxin A. Results support further evaluation of this chimeric *protein"** as a vaccine to prevent Pseudomonas colonization in susceptible individuals.

8/3,AB/7 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

12710444 GENUINE ARTICLE#: 432MG NUMBER OF REFERENCES: 26
TITLE: A recombinant chimera composed of *repeat"** region RR1 of Mycoplasma hyopneumoniae adhesin with Pseudomonas exotoxin: in vivo evaluation of specific IgG response in mice and pigs
AUTHOR(S): Chen JR; Liao CW; Mao SJT; Weng CN (REPRINT)
AUTHOR(S) E-MAIL: cnw01@vax1.prit.org.tw
CORPORATE SOURCE: Pig Res Inst Taiwan, Dept Pathobiol, POB 23/Chunan Miaoli 35099//Taiwan/ (REPRINT); Pig Res Inst Taiwan, Dept Pathobiol, /Chunan Miaoli 35099//Taiwan/
PUBLICATION TYPE: JOURNAL
PUBLICATION: VETERINARY MICROBIOLOGY, 2001, V80, N4 (JUN 22), P347-357
PUBLISHER: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS
ISSN: 0378-1135
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: Using the binding and translocation domain of *Pseudomonas"** *exotoxin"** *A"** [domain III deleted PE termed PE(Delta III)] as a vehicle, this study characterized and evaluated a novel application of PE toxin in Mycoplasma hyopneumoniae adhesin used as an immunogen. PCR and sequence analysis revealed that 16 *copies"** of AAKPV(E) in tandem *repeat"** region 1 (RR1) of M. hyopneumoniae 97 kDa adhesion were successfully fused to the downstream of PE(Delta III) to create a subunit vaccine, i.e. PE(Delta III)-RR1. This chimeric *protein"**, over-expressed in inclusion bodies of E. coli BL21(DES)pLysS, was characterized by a monoclonal antibody (MAb) F2G5 prepared against RR1 of the 97 kDa adhesin and was readily purified. The data indicated that the epitope recognized by MAb F2G5 was located in the structure of PE(Delta III)-RR1. Using ELISA and Western blot analyses, the specific IgG immune response against RR1 and whole adhesin in mice immunized with PE(Delta III)-RR1 was found more marked than that in mice immunized with the M. hyopneumoniae whole cells. Similarly, PE(Delta III)-RR1 also stimulated a remarkable IgG response against RR1 in pigs compared to that in pigs immunized with the conventional M. hyopneumoniae vaccine. The PE(Delta III)-RR1 would be potentially useful for the future development of a M. hyopneumoniae adhesin vaccine.

8/3,AB/8 (Item 3 from file: 440)

DIALOG(R)File 440:Current Contents Search(R)

07817837 GENUINE ARTICLE#: VN180 NUMBER OF REFERENCES: 32
TITLE: Translocation of full-length Pseudomonas exotoxin from endosomes is drivenby ATP hydrolysis but requires prior exposure to acidic pH
AUTHOR(S): Taupiac MP; Alami M; Beaumelle B
CORPORATE SOURCE: UNIV MONTPELLIER 2,CNRS, UMR 5539, DEPT BIOL SANTE, CASE 107/F-34095 MONTPELLIER 5//FRANCE/ (REPRINT); UNIV MONTPELLIER 2,CNRS, UMR 5539, DEPT BIOL SANTE/F-34095 MONTPELLIER 5//FRANCE/
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF BIOLOGICAL CHEMISTRY, 1996, V271, N42 (OCT 18), P 26170-26173
PUBLISHER: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814
ISSN: 0021-9258
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: We attached human transferrin to *Pseudomonas"** *exotoxin"** *A"** (PE) to specifically localize this toxin to the endosomal compartment and study its translocation from purified endosomes using a cell-free assay, Transferrin was linked to PE via a disulfide bond, Chemical derivatization inactivated the PE cell-binding domain, and transferrin-PE was found to be endocytosed via the transferrin receptor only, Transferrin was also conjugated to a truncated PEwith no *receptor"**-*binding"** *domain"** (PE46). After labeling mouse lymphocytes with radiolabeled transferrin-PE or transferrin-PE46 and endosome isolation,selective translocation of the full-sized toxin portion of the conjugate was observed in a cell-free system, This translocation was strictly dependent upon ATP hydrolysis and was not affected when the acidity of the endosomelumen was neutralized using weak bases, protonophores, or bafilomycin A(1), Nevertheless, when present during cell labeling, inhibitors of endosome acidification prevented PE from acquiring translocation competence, Similar inhibition was observed when endocytosis was performed in the presence of brefeldin A, a drug known to interfere with the delivery of endocytic tracers to acidic endosomes, Our data indicate that full-length PE can be transferred to the cytosol directly from endosomes during intoxication by PE conjugates and that, although exposure to acidic pH is a prerequisite for translocation, ATP hydrolysis directly provides the energy required for PE translocation.

8/3,AB/9 (Item 4 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

05839795 GENUINE ARTICLE#: PK830 NUMBER OF REFERENCES: 78
TITLE: REFINED STRUCTURE OF DIMERIC DIPHTHERIA TOXIN AT 2.0 ANGSTROM RESOLUTION
AUTHOR(S): BENNETT MJ; CHOE S; EISENBERG D (Reprint)
CORPORATE SOURCE: UNIV CALIF LOS ANGELES,INST MOLEC BIOL,DEPT CHEM & BIOCHEM/LOS ANGELES//CA/90024 (Reprint); UNIV CALIF LOS ANGELES,INST MOLEC BIOL,DEPT CHEM & BIOCHEM/LOS ANGELES//CA/90024; UNIV CALIF LOS ANGELES,UCLA DOE,STRUCT BIOL & MOLEC MED LAB/LOS ANGELES//CA/90024
PUBLICATION: PROTEIN SCIENCE, 1994, V3, N9 (SEP), P1444-1463
ISSN: 0961-8368
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE
ABSTRACT: The refined structure of dimeric diphtheria toxin (DT) at 2.0

Angstrom resolution, based on 37,727 unique reflections (F> 1 sigma(F)), yields a final R factor of 19.5% with a model obeying standard geometry. The refined model consists of 523 amino acid residues, 1 molecule of the bound dinucleotide inhibitor adenylyl 3'-5' uridine 3' monophosphate (ApUp), and 405 well-ordered water molecules. The 2.0-Angstrom refined model reveals that the binding motif for ApUp includes residues in the catalytic and *receptor"**-*binding"** *domains"** and is different from the Rossmann dinucleotide-binding fold. ApUp is bound in part by a long loop (residues 34-52) that crosses the active site. Several residues in the active site were previously identified as NAD-binding residues. Glu 148, previously identified as playing a catalytic role in ADP-ribosylation of elongation factor 2 by DT, is about 5 Angstrom from uracil in ApUp. The trigger for insertion of the transmembrane domain of DT into the endosomal membrane at low pH may involve 3 intradomain and 4 interdomain salt bridges that will be weakened at low pH by protonation of their acidic residues. The refined model also reveals that each molecule in dimeric DT has an ''open'' structure unlike most globular *proteins"**, which we call an open monomer. Two open monomers interact by ''domain swapping'' to form a compact, globular dimeric DT structure. The possibility that the open monomer resembles a membrane insertion intermediate is discussed.

8/3,AB/10 (Item 5 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

03689321 GENUINE ARTICLE#: HV195 NUMBER OF REFERENCES: 50
TITLE: THE CRYSTAL STRUCTURE OF DIPHTHERIA TOXIN
AUTHOR(S): CHOE S; BENNETT MJ; FUJII G; CURMI PMG; KANTARDJIEFF KA; COLLIER RJ; EISENBERG D
CORPORATE SOURCE: UNIV CALIF LOS ANGELES,INST MOLEC BIOL/LOS ANGELES//CA/90024 (Reprint); UNIV CALIF LOS ANGELES,DEPT CHEM & BIOCHEM/LOS ANGELES//CA/90024; HARVARD UNIV,SCH MED,SHIPLEY INST MED,DEPT MICROBIOL & MOLEC GENET/BOSTON//MA/02115
PUBLICATION: NATURE, 1992, V357, N6375 (MAY 21), P216-222
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE
ABSTRACT: The crystal structure of the diphtheria toxin dimer at 2.5 angstrom resolution reveals a Y-shaped molecule of three domains. The catalytic domain, called fragment A, is of the alpha + beta-type. Fragment B actually consists of two domains. The transmembrane domain consists of nine alpha-helices, two pairs of which are unusually apolar and may participate in pH-triggered membrane insertion and translocation. The *receptor"**-*binding"** *domain"** is a flattened beta-barrel with a jelly-roll-like topology. Three distinct functions of the toxin, each carried out by a separate structural domain, can be useful in designing chimaeric *proteins"**, such as immunotoxins, in which the *receptor"**-*binding"** *domain"** is substituted with antibodies to target other cell types.

8/3,AB/11 (Item 6 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

03559299 GENUINE ARTICLE#: HK753 NUMBER OF REFERENCES: 44
TITLE: LYMPHOPROLIFERATIVE ACTIVITY OF *PSEUDOMONAS"** *EXOTOXIN"**-*A"**

IS DEPENDENT ON INTRACELLULAR PROCESSING AND IS ASSOCIATED WITH THE CARBOXYL-TERMINAL PORTION
AUTHOR(S): LEGAARD PK; LEGRAND RD; MISFELDT ML (Reprint)
CORPORATE SOURCE: UNIV MISSOURI,SCH MED,DEPT MOLEC MICROBIOL & IMMUNOL/COLUMBIA//MO/65212 (Reprint); UNIV MISSOURI,SCH MED,DEPT MOLEC MICROBIOL & IMMUNOL/COLUMBIA//MO/65212
PUBLICATION: INFECTION AND IMMUNITY, 1992, V60, N4 (APR), P1273-1278
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE
ABSTRACT: *Pseudomonas"** aeruginosa *exotoxin"** *A"** (PE) represents a microbial superantigen that requires processing by accessory cells in order to induce the proliferation of V(beta)8-bearing murine T lymphocytes. In this study, we have observed that PE requires intracellular processing by a protease in order to induce lymphoproliferation. Pepstatin A, an inhibitor of acid proteases, inhibited PE-induced lymphoproliferation, whereas leupeptin, an inhibitor of serine and thiol proteases, had no effect on PE-induced lymphoproliferation. A number of mutant forms of PE were examined for their ability to induce lymphoproliferation. The mutant form which lacks amino acids 5 to 224 of the *receptor"**-*binding"** *domain"**, PE43, was capable of inducing murine thymocytes to proliferate in the presence of accessory cells. However, neither PEgly276, a mutant toxin which undergoes a different intracellular processing pattern than wild-type PE, nor PE589, a mutant toxin which lacks amino acids 590 to 613 at the carboxyl terminus, was able to induce thymocyte proliferation. In addition, the lymphoproliferation induced by the PE43 mutant form of PE could also be inhibited by pepstatin A. Therefore, our data indicate that intracellular processing by a proteolytic enzyme which is inhibited by pepstatin A is critical for PE-induced lymphoproliferation. Furthermore, the lymphoproliferative activity of PE is associated with the carboxyl-terminal portion of PE.

8/3,AB/12 (Item 7 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

02817560 GENUINE ARTICLE#: FL585 NUMBER OF REFERENCES: 22
TITLE: FUNCTIONAL ANALYSIS OF *EXOTOXIN"** *A"**-RELATED *PROTEIN"** OF *PSEUDOMONAS"**-AERUGINOSA LACKING RESIDUES 225-412
AUTHOR(S): GUIDIRONTANI C
CORPORATE SOURCE: INST PASTEUR,CNRS,URA 557,UNITE ANTIGENES BACTERIENS/F-75724 PARIS 15//FRANCE/ (Reprint); HARVARD UNIV,SCH MED,DEPT MICROBIOL & MOLEC GENET/BOSTON//MA/02115; SHIPLEY INST MED/BOSTON//MA/00000
PUBLICATION: FEMS MICROBIOLOGY LETTERS, 1991, V80, N1 (MAY 1), P103-109
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE
ABSTRACT: The crystal structure of the *exotoxin"** *A"** (ETA) of *Pseudomonas"** aeruginosa showed that this *protein"** is folded into three distinct domains. Domain I (Ia and Ib), the amino-terminal domain, is the *receptor"**-*binding"** *domain"** of ETA and domain III, the carboxy-terminal domain, is responsible for the ADP-ribosyl transferase activity of the toxin. To elucidate the function(s) of domains 1b and II in the intoxication process and to define the region of the domain III necessary for ADP-ribosylating activity, a defined deletion in the structural gene of P. aeruginosa ETA encompassing residues 225-412 was constructed and an ETA-related product DeID, (from which all of domains II and Ib were deleted) was expressed. The ETA-related *protein"** did not penetrate sensitive cells, but retained

the same specific activity to ADP-ribosylate elongation factor-2 as wild-type toxin. This suggests that domain II is necessary to allow toxin internalization by sensitive cells and that the absence of domain Ib does not interfere with enzymic activity. The domain strictly involved in ADP-ribosylation activity encompasses residues 412-613.

8/3,AB/13 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01277862
Simultaneous detection, identification and differentiation of Eubacterial taxa using a hybridization assay
Gleichzeitiger Nachweis, Identifizierung und Differenzierung von Eubakterien unter Verwendung eines Hybridisierungs-Assays
Detection, identification et differentiation simultanees de taxa d'eubacteriales a l'aide d'une technique d'hybridation
PATENT ASSIGNEE:
INNOGENETICS N.V., (713142), Industriepark Zwijnaarde 7, Box 4, 9052 Gent , (BE), (Applicant designated States: all)
INVENTOR:
Jannes, Geert, E. van Hoorenbekelaan 23, P.O. Box 1, 3010 Kessel-Lo, (BE)
Rossau, Rudi, Wilgehoevestraat 45, 2180 Ekeren, (BE)
Van Heuverswyn, Hugo, Colmanstraat 80, 9270 Kalken, (BE)
PATENT (CC, No, Kind, Date): EP 1098007 A1 010509 (Basic)
APPLICATION (CC, No, Date): EP 1200046 950623;
PRIORITY (CC, No, Date): EP 94870106 940624; EP 95870032 950407
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 769068 (EP 95924923)
INTERNATIONAL PATENT CLASS: C12Q-001/68

ABSTRACT EP 1098007 A1
The present invention relates to a method for detection and identification of at least one micro-organism, or for the simultaneous detection of several micro-organisms in a sample, comprising the steps of:
(i) if need be releasing, isolating or concentrating the polynucleic acids present in the sample;
(ii) if need be amplifying the 16S-23S rRNA spacer region, or a part of it, with at least one suitable primer pair;
(iii) hybridizing the polynucleic acids of step (i) or (ii) with at least one and preferably more than one of the spacer probes as mentioned in table 1a or equivalents of thereof, under the appropiate hybridization and wash conditions, and/or with a taxon-specific probe derived from any of the spacer sequences as represented in figs. 1-103 under the same hybridization and wash conditions;
(iv) detecting the hybrids formed in step (iii) with each of the probes used under appropiate hybridization and wash conditions;
(v) identification of the micro-organism(s) present in the sample from the differential hybridization signals obtained in step (iv).
ABSTRACT WORD COUNT: 175
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200119	820
SPEC A	(English)	200119	22652
Total word count - document A			23472
Total word count - document B			0
Total word count - documents A + B			23472

8/3,AB/14 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01277861
Simultaneous detection, identification and differentiation of eubacterial taxa using a hybridization assay
Gleichzeitiger Nachweis, Identifizierung und Differenzierung von Eubakterien unter Verwendung eines Hybridisierungs-Assays
Detection, identification et differentiation simultanees de taxa d'eubacteriales a l'aide d'une technique d'hybridation

PATENT ASSIGNEE:
INNOGENETICS N.V., (713142), Industriepark Zwijnaarde 7, Box 4, 9052 Gent , (BE), (Applicant designated States: all)
INVENTOR:
Jannes, Geert, E. Van Hoorenbekelaan 23, P.O. Box 1, 3010 Kessel-Lo, (BE)
Rossau, Rudi, Wilgehoevestraat 45, 2180 Ekeren, (BE)
Van Heuverswyn, Hugo, Colmanstraat 80, 9270 Kalken, (BE)

PATENT (CC, No, Kind, Date): EP 1098006 A1 010509 (Basic)
APPLICATION (CC, No, Date): EP 1200045 950623;
PRIORITY (CC, No, Date): EP 94870106 940624; EP 95870032 950407
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: LT; LV; SI
RELATED PARENT NUMBER(S) - PN (AN):
EP 769068 (EP 95924923)
INTERNATIONAL PATENT CLASS: C12Q-001/68

ABSTRACT EP 1098006 A1

The present invention relates to a method for detection and identification of at least one micro-organism, or for the simultaneous detection of several micro-organisms in a sample, comprising the steps of:

(i) if need be releasing, isolating or concentrating the polynucleic acids present in the sample;

(ii) if need be amplifying the 16S-23S rRNA spacer region, or a part of it, with at least one suitable primer pair;

(iii) hybridizing the polynucleic acids of step (i) or (ii) with at least one and preferably more than one of the spacer probes as mentioned in table 1a or equivalents of thereof, under the appropiate hybridization and wash conditions, and/or with a taxon-specific probe derived from any of the spacer sequences as represented in figs. 1-103 under the same hybridization and wash conditions;

(iv) detecting the hybrids formed in step (iii) with each of the probes used under appropiate hybridization and wash conditions;

(v) identification of the micro-organism(s) present in the sample from the differential hybridization signals obtained in step (iv).

ABSTRACT WORD COUNT: 175
NOTE:

Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200119	623
SPEC A	(English)	200119	22683
Total word count - document A			23306
Total word count - document B			0
Total word count - documents A + B			23306

8/3,AB/15 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01266800
Simultaneous detection, identification and differentiation of Eubacterial taxa using a hybridization assay
Gleichzeitiger Nachweis, Identifizierung und Differenzierung von Eubakterien unter Verwendung eines Hybridisierungs-Assays
Detection, identification et differentiation simultanees de taxa d'eubacteriales a l'aide d'une technique d'hybridation
PATENT ASSIGNEE:
INNOGENETICS N.V., (713142), Industriepark Zwijnaarde 7, Box 4, 9052 Gent , (BE), (Applicant designated States: all)
INVENTOR:
Jannes, Geert, E. Van Hoorenbekelaan 23, P.O. Box 1, 3010 Kessel-Lo, (BE)
Rossau, Rudi, Wilgehoevestraat 45, 2180 Ekeren, (BE)
Van Heuverswyn, Hugo, Colmanstraat 80, 9270 Kalken, (BE)
PATENT (CC, No, Kind, Date): EP 1091004 A2 010411 (Basic)
EP 1091004 A3 010418
APPLICATION (CC, No, Date): EP 1200042 950624;
PRIORITY (CC, No, Date): EP 94870106 940624; EP 95870032 950407
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 769068 (EP 95924923)
INTERNATIONAL PATENT CLASS: C12Q-001/68

ABSTRACT EP 1091004 A3
The present invention relates to a method for detection and identification of at least one micro-organism, or for the simultaneous detection of several micro-organisms in a sample, comprising the steps of:
(i) if need be releasing, isolating or concentrating the polynucleic acids present in the sample;
(ii) if need be amplifying the 16S-23S rRNA spacer region, or a part of it, with at least one suitable primer pair;
(iii) hybridizing the polynucleic acids of step (i) or (ii) with at least one and preferably more than one of the spacer probes as mentioned in table 1a or equivalents of thereof, under the appropriate hybridization and wash conditions, and/or with a taxon-specific probe derived from any of the spacer sequences as represented in figs. 1-103 under the same hybridization and wash conditions;
(iv) detecting the hybrids formed in step (iii) with each of the probes used under appropriate hybridization and wash conditions;
(v) identification of the micro-organism(s) present in the sample from

the differential hybridization signals obtained in step (iv).
ABSTRACT WORD COUNT: 175
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200115	1775
SPEC A	(English)	200115	22666
Total word count - document A			24441
Total word count - document B			0
Total word count - documents A + B			24441

8/3,AB/16 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01264867
*Peptide"** *repeat"** immunogens
Immunogene mit *repetitiver"** Peptidsequenzen
Immunogenes a sequences peptidiques *repetitives"**
PATENT ASSIGNEE:
Academia Sinica, (2170752), 128 Sec. 2, Yen Chiu Yuan Road, Nan-Kang, Taipei, 115, (TW), (Applicant designated States: all)
INVENTOR:
Hwang, Jaulang, 3F, no.20-1,Alley 3, Lane 61, Sec 2,Enjoyean Road, Nankang Taipei, (TW)
Hsu, Chia-Tse, 2F, no. 67, Ku-Dse-Tou, Shi-Kang, Tainan, (TW)
Ting, Chun-Jen, 3F, no. 29, Lane 172, Sec. 2, Donda Road, Hsinchu, (TW)
LEGAL REPRESENTATIVE:
Woods, Geoffrey Corlett (48721), J.A. KEMP & CO. Gray's Inn 14 South Square, London WC1R 5JJ, (GB)
PATENT (CC, No, Kind, Date): EP 1090994 A2 010411 (Basic)
EP 1090994 A3 010718
APPLICATION (CC, No, Date): EP 2000304253 000519;
PRIORITY (CC, No, Date): US 412558 991005
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12N-015/31; C12N-015/39; C12N-015/16; C12N-015/62; A61K-048/00; A61K-039/00; A61K-039/104; A61K-039/285; A61K-039/295; A61K-038/09; C07K-007/23; C07K-014/21; C07K-014/07

ABSTRACT EP 1090994 A2
A *polypeptide"** comprising, (1) a *receptor"** *binding"** *domain"** of a *Pseudomonas"** *exotoxin"** *A"** or a functional variant thereof, and (2) at least two *copies"** of a *peptide"** sequence.
ABSTRACT WORD COUNT: 29
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200115	204
SPEC A	(English)	200115	3906

Total word count - document A 4110
Total word count - document B 0
Total word count - documents A + B 4110

8/3,AB/17 (Item 5 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01264158
Simultaneous detection, identification and differentiation of Eubacterial taxa using a hybridization assay
Gleichzeitiger Nachweis, Identifizierung und Differenzierung von Eubakterien unter Verwendung eines Hybridisierungs-Assays
Detection, identification et differentiation simultanees de taxa d'eubacteriales a l'aide d'une technique d'hybridation
PATENT ASSIGNEE:
N.V. INNOGENETICS S.A., (713141), Industriepark Zwijnaarde 7, Box 4, 9052 Gent, (BE), (Applicant designated States: all)
INVENTOR:
Jannes, Geert, E. van Hoorenbekelaan 23, P.O. Box 1, 3010 Kessel-Lo, (BE)
Rossau, Rudi, Wilgehoevestraat 45, 2180 Ekeren, (BE)
Van Heuverswyn, Hugo, Colmanstraat 80, 9270 Kalken, (BE)
PATENT (CC, No, Kind, Date): EP 1088899 A2 010404 (Basic)
EP 1088899 A3 010502
APPLICATION (CC, No, Date): EP 1200037 950623;
PRIORITY (CC, No, Date): EP 94870106 940624; EP 95870032 950407
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: LT; LV; SI
RELATED PARENT NUMBER(S) - PN (AN):
EP 769068 (EP 95924923)
INTERNATIONAL PATENT CLASS: C12Q-001/68

ABSTRACT EP 1088899 A3

The present invention relates to a method for detection and identification of at least one micro-organism, or for the simultaneous detection of several micro-organisms in a sample, comprising the steps of:

(i) if need be releasing, isolating or concentrating the polynucleic acids present in the sample;

(ii) if need be amplifying the 16S-23S rRNA spacer region, or a part of it, with at least one suitable primer pair;

(iii) hybridizing the polynucleic acids of step (i) or (ii) with at least one and preferably more than one of the spacer probes as mentioned in table 1a or equivalents of thereof, under the appropiate hybridization and wash conditions, and/or with a taxon-specific probe derived from any of the spacer sequences as represented in figs. 1-103 under the same hybridization and wash conditions;

(iv) detecting the hybrids formed in step (iii) with each of the probes used under appropiate hybridization and wash conditions;

(v) identification of the micro-organism(s) present in the sample from the differential hybridization signals obtained in step (iv).

ABSTRACT WORD COUNT: 175

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:
Available Text Language Update Word Count

CLAIMS A	(English)	200114	792
SPEC A	(English)	200114	22587
Total word count - document A			23379
Total word count - document B			0
Total word count - documents A + B			23379

8/3,AB/18 (Item 6 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01250693
Pseudomonas fusion *protein"** vaccines
Pseudomonas *Fusionsprotein"**-Impstoff
Vaccins a base de proteines de fusion de Pseudomonas
PATENT ASSIGNEE:
Academia Sinica, (2170752), 128 Sec. 2, Yen Chiu Yuan Road, Nan-Kang, Taipei, 115, (TW), (Applicant designated States: all)
INVENTOR:
Hwang, Jaulang, 3F,No. 20-1,Alley 3,Lane 61, Sec.2, Enjoyean Road, Nankang, Taipei, (TW)
Shang, Huey-Fang, 5F,No.5,Alley 12,Lane 15,Sec 6, Sin-Yi Road, Taipei, (TW)
Chen, Tzong-Yueh, No.7, Lane 345, Yu-Ron Road, Tainan, (TW)
LEGAL REPRESENTATIVE:
Woods, Geoffrey Corlett (48721), J.A. KEMP & CO. Gray's Inn 14 South Square, London WC1R 5LX, (GB)
PATENT (CC, No, Kind, Date): EP 1078988 A1 010228 (Basic)
APPLICATION (CC, No, Date): EP 99306862 990827;
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12N-015/31; C07K-014/21; C12N-015/79; C12N-005/10; C07K-019/00; C12N-015/62; A61K-039/104; A61K-048/00

ABSTRACT EP 1078988 A1
A *polypeptide"** comprises segments:
(1) a *receptor"** *binding"** *domain"** of a Pseudomonas exotoxin or functional variant thereof;
(2) a membrane translocation domain of a Pseudomonas exotoxin or functional variant thereof;
(3) a Pseudomonas *lipoprotein"** I or functional variant thereof, or antigenic fragment of a Pseudomonas *lipoprotein"** I or functional variant thereof; and
(4) an antigenic C-terminal fragment of a Pseudomonas porin *protein"** F or functional variant thereof.
The *polypeptide"** is useful in vaccine compositions.
ABSTRACT WORD COUNT: 79

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200109	465
SPEC A	(English)	200109	4677
Total word count - document A			5142
Total word count - document B			0
Total word count - documents A + B			5142

8/3,AB/19 (Item 7 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01123403
Recombinant alphavirus vectors
Rekombinante Alphavirus Vektoren
Vecteurs composes d'alphavirus recombinants
PATENT ASSIGNEE:
CHIRON CORPORATION, (572530), 4560 Horton Street, Emeryville, California 94608, (US), (Applicant designated States: all)
INVENTOR:
Dubensky, Thomas W. Jr., P.O. Box 802, Del Mar, CA 92014, (US)
Ibanez, Carlos E., 13592 Millpond Way, San Diego, CA 92129, (US)
Chang, Stephen M.W., 12912 Camino del Valle, Poway, CA 92064, (US)
Jolly, Douglas J., 277 Hillcrest Drive, Leucadia, CA 92024, (US)
Driver, David A., 1015 Santa Estrella, Solana Beach, California 92075, (US)
Polo, John M., 221 Witham Road, Encinitas, CA 92024, (US)
LEGAL REPRESENTATIVE:
Hallybone, Huw George et al (53031), CARPMAELS AND RANSFORD 43 Bloomsbury Square, London WC1A 2RA, (GB)
PATENT (CC, No, Kind, Date): EP 982405 A2 000301 (Basic)
EP 982405 A3 000412
APPLICATION (CC, No, Date): EP 99102370 940915;
PRIORITY (CC, No, Date): US 122791 930915; US 198450 940218
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 694070 (EP 94929221)
INTERNATIONAL PATENT CLASS: C12N-015/86; C12N-005/10; A61K-035/76; A61K-048/00

ABSTRACT EP 982405 A2
The present invention provides compositions and methods for utilizing recombinant alphavirus particles. In particular, it provides a recombinant alphavirus particle which is free from contaminating wild-type alphavirus particles.
ABSTRACT WORD COUNT: 29
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200009	857
SPEC A	(English)	200009	60726
Total word count - document A			61583
Total word count - document B			0
Total word count - documents A + B			61583

8/3,AB/20 (Item 8 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01069070

Humanized antibody variable domain
Anderliches Gebiet einer humanisierter Antikorper
Domaine variable d'un anticorps humanise
PATENT ASSIGNEE:
  Genentech, Inc., (210486), 1 DNA Way, South San Francisco, CA 94080-4990, (US), (Applicant designated States: all)
INVENTOR:
  Carter, Paul J., 1048 Monterey Blvd., San Francisco, CA 94127, (US)
  Presta, Leonard G., 1900 Gough Street, 206, San Francisco, CA 94109, (US)
LEGAL REPRESENTATIVE:
  Barz, Peter, Dr. (1467), Patentanwalt Kaiserplatz 2, 80803 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 940468 A1 990908 (Basic)
APPLICATION (CC, No, Date): EP 99105252 920615;
PRIORITY (CC, No, Date): US 715272 910614
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; MC; NL; SE
RELATED PARENT NUMBER(S) - PN (AN):
  EP 590058 (EP 92914220)
INTERNATIONAL PATENT CLASS: C12N-015/13; C12P-021/08; C12N-005/10; G06F-015/00; C07K-016/28; C07K-016/46

ABSTRACT EP 940468 A1
  Described is a humanized antibody variable domain having a non-human Complementarity Determining Region (CDR) incorporated into a human antibody variable domain and further comprising an amino acid substitution at a site selected from the group consisting of: 4L, 35L, 36L, 38L, 43L, 44L, 46L, 58L, 62L, 64L, 65L, 66L, 67L, 68L, 69L, 70L, 71L, 73L, 85L, 87L, 98L, 2H, 4H, 24H, 36H, 37H, 39H, 43H, 45H, 49H, 68H, 69H, 70H, 73H, 74H, 75H, 76H, 78H, 92H, and 93H.
ABSTRACT WORD COUNT: 79
NOTE:
  Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9936	131
SPEC A	(English)	9936	31476
Total word count - document A			31607
Total word count - document B			0
Total word count - documents A + B			31607

8/3,AB/21 (Item 9 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00948803
Corticotropin-releasing factor2 receptors
Corticotropin freisetzende Rezeptoren des Faktor 2
Recepteurs du facteur 2 liberant la corticotropine
PATENT ASSIGNEE:
  NEUROCRINE BIOSCIENCES, INC., (1942291), 3050 Science Park Road, San Diego, CA 92121-1102, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
  Lovenberg, Timothy W., 6529 Vispera Place, Carlsbad California 92009, (US)

Oltersdorf, Tilman, 427 Bristol Avenue, Cardiff California 92007, (US)
Liaw, Chen Wang, 7668 Sallx Place, San Diego California 92129, (US)
Grigoriadis, Dimitri E., 2831 Vista Mariana, Carlsbad California 92009, (US)
Chalmers, Derek T., 347 Longdon Lane, Solana Beach California 92075, (US)
Desouza, Errol B., 4507 South Lane, Del Mar California 92014, (US)
LEGAL REPRESENTATIVE:
Gowshall, Jonathan Vallance et al (61531), FORRESTER & BOEHMERT Franz-Joseph-Strasse 38, 80801 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 860501 A2 980826 (Basic)
EP 860501 A3 990519
APPLICATION (CC, No, Date): EP 98104491 950614;
PRIORITY (CC, No, Date): US 259959 940614
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 724637 (EP 959252719)
INTERNATIONAL PATENT CLASS: C12N-015/12; C12N-015/83; C12N-005/10; C07K-014/72; C07K-016/28; C12Q-001/68; C12Q-001/00; A61K-038/17;

ABSTRACT EP 860501 A2
The present invention provides isolated nucleic acid molecules encoding CRF2 receptors, recombinant expression vectors and host cells suitable for expressing such receptors, as well as compositions and methods which utilize such receptors.
ABSTRACT WORD COUNT: 33

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9835	1155
SPEC A	(English)	9835	23151
Total word count - document A			24306
Total word count - document B			0
Total word count - documents A + B			24306

8/3,AB/22 (Item 10 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00891422
Recombinant alphavirus vectors
Rekombinante Alphavirus-Vektoren
Vecteurs composes d'alphavirus recombinants
PATENT ASSIGNEE:
CHIRON CORPORATION, (572530), 4560 Horton Street, Emeryville, California 94608, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
Dubensky, Thomas W. Jr., P.O.Box 802elino, Del Mar, CA 92014, (US)
Ibanez, Carlos E., 13592 Millpond Way, San Diego, CA 92129, (US)
Chang, Stephen M.W., 12912 Camino del Valle, Poway, California 92064, (US)
Jolly, Douglas J., 277 Hillcrest Drive, leucadia, CA 92024, (US)
Driver, David A., 5142 Biltmore St., San Diego, CA 92117, (US)
Polo, John M., 221 Witham Road, Encinitas, CA 92024, (US)
LEGAL REPRESENTATIVE:

Hallybone, Huw George et al (53031), CARPMAELS AND RANSFORD 43 Bloomsbury Square, London WC1A 2RA, (GB)
PATENT (CC, No, Kind, Date): EP 814154 A2 971229 (Basic)
EP 814154 A3 981014
APPLICATION (CC, No, Date): EP 97113527 940915;
PRIORITY (CC, No, Date): US 122791 930915; US 198450 940218
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 694070 (EP 949292213)
INTERNATIONAL PATENT CLASS: C12N-007/01; C12N-015/86;

ABSTRACT EP 814154 A2
The present invention provides expression cassettes for expression of alphavirus structural *proteins"** and host cells, including packaging cells for packaging of alphavirus RNA vectors, containing such expression cassettes.
ABSTRACT WORD COUNT: 29

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9712W3	740
SPEC A	(English)	9712W3	61597
Total word count - document A			62337
Total word count - document B			0
Total word count - documents A + B			62337

8/3,AB/23 (Item 11 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00825306
DNA SEQUENCE AND ENCODED MAMMARY-SPECIFIC BREAST CANCER *PROTEIN"**
DNS-SEQUENZ UND KODIERTES BRUSTDRUSENSPEZIFISISCHES *BRUSTKREBSPROTEIN"**
SEQUENCE D'ADN ET *PROTEINE"** CODEE DU CANCER DU SEIN SPECIFIQUE DE LA GLANDE MAMMAIRE
PATENT ASSIGNEE:
WASHINGTON UNIVERSITY, (645448), 1 Brookings Drive, St. Louis, MO 63130, (US), (Proprietor designated states: all)
INVENTOR:
WATSON, Mark, A., 1461 Meadowside Drive, St. Louis, MO 63146, (US)
FLEMING, Timothy, P., 743 Eaglebrooke Drive, St. Louis, MO 63021, (US)
LEGAL REPRESENTATIVE:
Brock, Peter William et al (28726), Urquhart-Dykes & Lord 1 Richfield Place Richfield Avenue, Reading RG1 8EQ Berkshire, (GB)
PATENT (CC, No, Kind, Date): EP 833834 A1 980408 (Basic)
EP 833834 A1 980603
EP 833834 B1 000308
WO 9638463 961205
APPLICATION (CC, No, Date): EP 96916892 960531; WO 96US8235 960531
PRIORITY (CC, No, Date): US 455896 950531
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C07H-021/04; C12Q-001/68; G01N-033/574
NOTE:
No A-document published by EPO

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200010	776
CLAIMS B	(German)	200010	761
CLAIMS B	(French)	200010	907
SPEC B	(English)	200010	8109
Total word count - document A			0
Total word count - document B			10553
Total word count - documents A + B			10553

8/3,AB/24 (Item 12 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00775369
NUCLEIC ACID TRANSFER SYSTEM
NUKLEINSAURE-EINBRINGUNGSSYSTEM
SYSTEME DE TRANSFERT DE L'ACIDE NUCLEIQUE
PATENT ASSIGNEE:
Wels, Winfried, (2051071), Bonner Weg 7, 63110 Rodgau, (DE), (Proprietor designated states: all)
INVENTOR:
WELS, Winfried, Glimpenheimer Strasse 55, D-79312 Emmendingen, (DE)
FOMINAYA, Jesus, Maulbeerstrasse 71, CH-4058 Basel, (CH)
LEGAL REPRESENTATIVE:
Keller, Gunter, Dr. et al (59792), Lederer, Keller & Riederer Patentanwalte Prinzregentenstrasse 16, 80538 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 789776 A1 970820 (Basic)
EP 789776 B1 010613
WO 9613599 960509
APPLICATION (CC, No, Date): EP 95937039 951031; WO 95EP4270 951031
PRIORITY (CC, No, Date): EP 94810627 941101
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/87; C12N-015/62; A61K-038/16; C12N-005/10
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200124	495
CLAIMS B	(German)	200124	441
CLAIMS B	(French)	200124	579
SPEC B	(English)	200124	21145
Total word count - document A			0
Total word count - document B			22660
Total word count - documents A + B			22660

8/3,AB/25 (Item 13 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00762297
Recombinant alphavirus vectors

Rekombinanter Alphavirus Vektor
Vecteurs composes d'alphavirus recombinants
PATENT ASSIGNEE:
  CHIRON VIAGENE, INC., (2076910), 4560 Horton Street, Emeryville,
    California 94608, (US), (applicant designated states:
    AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
  Dubensky, Thomas W. Jr., 12729 Via Felino, Del Mar, CA 92014, (US)
  Ibanez, Carlos E., 13592 Millpond Way, San Diego, CA 92129, (US)
  Chang, Stephen M.W., 9838 Via Cacares, San Diego, CA 92129, (US)
  Jolly, Douglas J., 277 Hillcrest Drive, Leucadia, CA 92024, (US)
  Driver, David A., 5142 Biltmore St., San Diego, CA 92117, (US)
  Polo, John M., 3910 Haines Street, No. 4, San Diego, CA 92109, (US)
LEGAL REPRESENTATIVE:
  Hallybone, Huw George et al (53031), CARPMAELS AND RANSFORD 43 Bloomsbury
    Square, London WC1A 2RA, (GB)
PATENT (CC, No, Kind, Date): EP 716148 A2 960612 (Basic)
                             EP 716148 A3 970102
APPLICATION (CC, No, Date): EP 95115460 940915;
PRIORITY (CC, No, Date): US 122791 930915; US 198450 940218
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC;
  NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
  EP 694070 (EP 949292213)
INTERNATIONAL PATENT CLASS: C12N-015/86;

ABSTRACT EP 716148 A2
    The present invention provides composition and methods for utilizing
  recombinant alphavirus vectors.
ABSTRACT WORD COUNT: 20

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB96	198
SPEC A	(English)	EPAB96	54363
Total word count - document A			54561
Total word count - document B			0
Total word count - documents A + B			54561

8/3,AB/26 (Item 14 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00756442
Recombinant alphavirus vectors
Rekombinanter Alphavirus Vektor
Vecteurs composes d'alphavirus recombinants
PATENT ASSIGNEE:
  CHIRON VIAGENE, INC., (2076910), 4560 Horton Street, Emeryville,
    California 94608, (US), (applicant designated states:
    AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
  Dubensky, Thomas W. Jr., 12729 Via Felino, Del Mar, CA 92014, (US)
  Ibanez, Carlos E., 13592 Millpond Way, San Diego, CA 92129, (US)
  Chang, Stephen M.W., 9838 Via Cacares, San Diego, CA 92129, (US)
  Jolly, Douglas H., 277 Hillcrest Drive, Leucadia, CA 92024, (US)

Driver, David H., 5142 Biltmore St., San Diego, CA 92117, (US)
Polo, John M., 221 Witham Road, Encinitas, CA 92024, (US)
LEGAL REPRESENTATIVE:
Brasnett, Adrian Hugh et al (73111), J.A. KEMP & CO. 14 South Square Gray's Inn, London WC1R 5LX, (GB)
PATENT (CC, No, Kind, Date): EP 711829 A2 960515 (Basic)
EP 711829 A3 970709
APPLICATION (CC, No, Date): EP 95115459 940915;
PRIORITY (CC, No, Date): US 122791 930915; US 198450 940218
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 694070 (EP 949292213)
INTERNATIONAL PATENT CLASS: C12N-007/01; C12N-015/86;

ABSTRACT EP 711829 A2
The present invention provides compositions and methods for utilizing recombinant alphavirus vectors.
ABSTRACT WORD COUNT: 20

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB96	1169
SPEC A	(English)	EPAB96	54372
Total word count - document A			55541
Total word count - document B			0
Total word count - documents A + B			55541

8/3,AB/27 (Item 15 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00748816
CORTICOTROPIN-RELEASING FACTOR 2 RECEPTORS
CORTICOTROPIN FREISETZENDE REZEPTOREN DES FAKTOR 2
RECEPTEURS DU FACTEUR 2 LIBERANT LA CORTICOTROPINE
PATENT ASSIGNEE:
NEUROCRINE BIOSCIENCES, INC., (1942291), 3050 Science Park Road, San Diego, CA 92121-1102, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
CHALMERS, Derek, 347 Longdon Lane, Solana Beach, CA 92075, (US)
LOVENBERG, Timothy W., 6529 Vispera Place, Carlsbad, CA 92009, (US)
OLTERSDORF, Tilman, 427 Bristol Avenue, Cardiff, CA 92007, (US)
LIAW, Chen Wang, 7668 Sallx Place, San Diego, CA 92129, (US)
GRIGORIADIS, Dimitri E., 2831 Vista Mariana, Carlsbad, CA 92009, (US)
DE SOUZA, Errol B., 4507 South Lane, Del Mar, CA 92014, (US)
LEGAL REPRESENTATIVE:
Armitage, Ian Michael et al (27761), MEWBURN ELLIS York House 23 Kingsway , London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 724637 A1 960807 (Basic)
EP 724637 B1 980916
WO 9534651 951221
APPLICATION (CC, No, Date): EP 95925271 950614; WO 95US7757 950614
PRIORITY (CC, No, Date): US 259959 940614; US 381433 950131; US 485984 950607

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/12; C07K-014/72; C07K-016/28; A61K-038/17; G01N-033/68; C12Q-001/68;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9838	1494
CLAIMS B	(German)	9838	1375
CLAIMS B	(French)	9838	1623
SPEC B	(English)	9838	23788
Total word count - document A			0
Total word count - document B			28280
Total word count - documents A + B			28280

8/3,AB/28 (Item 16 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00674686
Modification of pertussis toxin.
Modifizierung von Pertussistoxin.
Modification de la toxine pertussis.
PATENT ASSIGNEE:
CONNAUGHT LABORATORIES LIMITED, (267451), 1755 Steeles Avenue West, Willowdale Ontario M2R 3T4, (CA), (applicant designated states: DE;FR;GB)
THE UNIVERSITY OF ALBERTA, (1304291), Faculty of Pharmacy and Pharmaceutical Sciences, Edmonton, Alberta T6G 2N8, (CA), (applicant designated states: DE;FR;GB)
INVENTOR:
Armstrong, Glen D., 7951 91st Avenue, Edmonton, Alberta, (CA)
Read, Randy J., 10746 75th Avenue, Edmonton, Alberta T6E 1J9, (CA)
Oomen, Raymond, P.O. Box 10, R.R. 3, Tottenham, Ontario, (CA)
Hazes, Bart, 11012 82nd Avenue, Edmonton, Alberta, (CA)
Stein, Penelope E., 6 Great Eastern Street, Cambridge, (GB)
Loosmore, Sheena, 70 Crawford Rose Drive, Aurora, Ontario L4G 4R4, (CA)
Cockle, Stephen A., 159 Stephen Street, Richmond Hill, Ontario L2C 5P9, (CA)
Klein, Michel H., 16 Munro Boulevard, Willowdale, Ontario M2P 1B9, (CA)
LEGAL REPRESENTATIVE:
Smart, Peter John (43071), W.H. BECK, GREENER & CO 7 Stone Buildings Lincoln's Inn, London WC2A 3SZ, (GB)
PATENT (CC, No, Kind, Date): EP 646599 A2 950405 (Basic)
EP 646599 A3 960515
APPLICATION (CC, No, Date): EP 94306219 940823;
PRIORITY (CC, No, Date): US 110947 930824; US 251121 940531
DESIGNATED STATES: DE; FR; GB
INTERNATIONAL PATENT CLASS: C07K-014/235; G01N-033/569; G01N-033/566;

ABSTRACT EP 646599 A2
The three-dimensional structure of crystalline pertussis holotoxin (PT) has been determined by X-ray crystallography. Crystal structures have also been determined for complexes of pertussis toxin with molecules relevant to the biological activity of PT. These

three-dimensional structures were analysed to identify functional amino acids appropriate for modification to alter the biological properties of PT. Similar procedures may be used to predict amino acids which contribute to the toxicity of the holotoxin, to produce immunoprotective, genetically-detoxified analogs of pertussis toxin.
(see image in original document)
ABSTRACT WORD COUNT: 102

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB95	1713
SPEC A	(English)	EPAB95	13066
Total word count - document A			14779
Total word count - document B			0
Total word count - documents A + B			14779

8/3,AB/29 (Item 17 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00648931
ANTHRAX TOXIN FUSION *PROTEINS"** AND USES THEREOF
ANTHRAX-TOXIN-*FUSIONSPROTEINE"** UND DEREN VERWENDUNGEN
PROTEINES DE FUSION DE LA TOXINE DU BACILLE DU CHARBON ET LEURS UTILISATIONS
PATENT ASSIGNEE:
THE GOVERNMENT OF THE UNITED STATES OF AMERICA as represented by the SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES, (304190), National Institute of Health, Office of Technology Transfer, Westwood Building, Box OTT, Bethesda, MD 20892-9902, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
LEPPLA, Stephen H., 5612 Alta Vista Road, Bethesda, MD 20817, (US)
KLIMPEL, Kurt, 23816 Woodfield Road, Gaithersburg, MD 20882, (US)
ARORA, Naveen, G 110 Ashok Vihar, Phase I, Delhi 110052, (IN)
SINGH, Yogendra, SCIR Center for Biochemicals, University of Delhi, Mall Road, Delhi 110007, (IN)
LEGAL REPRESENTATIVE:
Thomson, Paul Anthony et al (36701), Potts, Kerr & Co. 15, Hamilton Square, Birkenhead Merseyside L41 6BR, (GB)
PATENT (CC, No, Kind, Date): EP 684997 A1 951206 (Basic)
EP 684997 B1 980819
WO 9418332 940818
APPLICATION (CC, No, Date): EP 94911385 940214; WO 94US1624 940214
PRIORITY (CC, No, Date): US 21601 930212; US 82849 930625
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/62; C12N-015/85; C12N-015/32; C07K-014/00; A61K-039/02; A61K-038/00;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9834	168
CLAIMS B	(German)	9834	134

CLAIMS B	(French)	9834	198
SPEC B	(English)	9834	21580
Total word count - document A			0
Total word count - document B			22080
Total word count - documents A + B			22080

8/3,AB/30 (Item 18 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00611010
DIPHTHERIA TOXIN RECEPTOR-BINDING REGION
REZEPTORBINDENDE REGION DES DIPHTHERIETOXIUS
REGION DE LIAISON DU RECEPTEUR DE LA TOXINE DE LA DIPHTERIE
PATENT ASSIGNEE:
THE PRESIDENT AND FELLOWS OF HARVARD COLLEGE, (227952), 17 Quincy Street, Cambridge, MA 02114, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
THE REGENTS OF THE UNIVERSITY OF CALIFORNIA, (221072), 300 Lakeside Drive, 22nd Floor, Oakland, California 94612-3550, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
COLLIER, R., John, 43 Garden Road, Wellesley Hills, MA 02181, (US)
EISENBERG, David, 342 Comstock Avenue, Los Angeles, CA 90024, (US)
FU, Haian, 65 Franklin Street, Allston, MA 02134, (US)
CHOE, Seunghyon, 7311 Darby Place, Reseda, CA 91335, (US)
LEGAL REPRESENTATIVE:
Baldock, Sharon Claire et al (73341), BOULT WADE TENNANT, 27 Furnival Street, London EC4A 1PQ, (GB)
PATENT (CC, No, Kind, Date): EP 643559 A1 950322 (Basic)
EP 643559 A1 970115
EP 643559 B1 990414
WO 9321769 931111
APPLICATION (CC, No, Date): EP 93911012 930503; WO 93US4166 930503
PRIORITY (CC, No, Date): US 881394 920506
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C07K-014/34;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9915	653
CLAIMS B	(German)	9915	561
CLAIMS B	(French)	9915	625
SPEC B	(English)	9915	8795
Total word count - document A			0
Total word count - document B			10634
Total word count - documents A + B			10634

8/3,AB/31 (Item 19 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00590797

Recombinant pseudomonas exotoxin: construction of an active immunotoxin with low side effects.
Rekombinantes Exotoxin von Pseudomonas: Konstruktion eines aktiven Immunotoxins mit schwachen Nebenwirkungen.
Exotoxine recombinante de Pseudomonas: construction d'une immunotoxine active avec effets secondaires faibles.

PATENT ASSIGNEE:
Pastan, Ira, (903100), 11710 Beall Mountain Road, Potamac Maryland 20854, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
Fitzgerald, David J., (903110), 1731 Ladd Street, Silver Spring Maryland 20902, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
Adhya, Sankar, (903120), 1440 Kings Grant Street, Gaithersbourg Maryland 20878, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Pastan, Ira, 11710 Beall Mountain Road, Potamac Maryland 20854, (US)
Fitzgerald, David J., 1731 Ladd Street, Silver Spring Maryland 20902, (US)
Adhya, Sankar, 1440 Kings Grant Street, Gaithersbourg Maryland 20878, (US)
LEGAL REPRESENTATIVE:
Patentanwalte Grunecker, Kinkeldey, Stockmair & Partner (100721), Maximilianstrasse 58, D-80538 Munchen, (DE)

PATENT (CC, No, Kind, Date): EP 583794 A1 940223 (Basic)
APPLICATION (CC, No, Date): EP 93113917 870923;
PRIORITY (CC, No, Date): US 911227 860924
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 261671 (EP 871139291)
INTERNATIONAL PATENT CLASS: C12N-015/00; A61K-039/104; A61K-037/00;

ABSTRACT EP 583794 A1
The present invention relates to various modified forms of Pseudomonas exotoxin exhibiting low toxicity to human or animal cells by itself but retaining its enzymatic activity. The modified Pseudomonas exotoxin of the present invention has ADP ribosylating activity but lacks all or part of domain II (responsible for translocation across cell membrane) of the native toxin. A preferred modified Pseudomonas exotoxin of the present invention further comprises a modification in the *receptor"** *binding"** *domain"** IA of the native Toxin. Conjugates (immunotoxins) comprising a modified Pseudomonas exotoxin and a targeting carrier, such as an antibody or a growth factor, methods for producing a modified Pseudomonas exotoxin or conjugates thereof and compositions suitable for administration to a mammal for achieving targeted cytotoxin activity are also disclosed.
ABSTRACT WORD COUNT: 126

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF2	638
SPEC A	(English)	EPABF2	4155
Total word count - document A			4793
Total word count - document B			0
Total word count - documents A + B			4793

8/3,AB/32 (Item 20 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00517216
Stable pura vectors and uses thereof
Stabile pura-Vektoren und ihre Verwendung
Vecteurs pura stables et leur utilisation
PATENT ASSIGNEE:
AMERICAN CYANAMID COMPANY, (212594), One Cyanamid Plaza, Wayne, NJ 07470-8426, (US), (Proprietor designated states: all)
INVENTOR:
Brey III, Robert Newton, 74 Sagamore Drive, Rochester, New York 14617, (US)
Fulginiti, James Peter, 5180 Foster Road, Canandaigua, New York 14424, (US)
Anilionis, Algis, 25 Whistlerhill Lane, Huntington, New York 11743, (US)
LEGAL REPRESENTATIVE:
Wachtershauser, Gunter, Prof. Dr. (12711), Patentanwalt, Tal 29, 80331 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 512260 A2 921111 (Basic)
EP 512260 A3 930728
EP 512260 B1 010704
APPLICATION (CC, No, Date): EP 92105887 920406;
PRIORITY (CC, No, Date): US 695706 910503
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/74; A61K-039/112; C12N-015/74; C12R-1:42

ABSTRACT EP 512260 A2
This invention pertains to a complementation system for the selection and maintenance of expressed genes in bacterial hosts. The invention provides stable vectors which can be selected and maintained by complementation of chromosomal deletion mutations of purA (adenylosuccinate synthetase), obviating the use of antibiotic resistance genes. This system is useful in production organisms during fermentation and in live vaccine bacteria, such as attenuated Salmonella typhi. This system allows for selection of chromosomal integrants and for selection and stable plasmid maintenance in the vaccinated host without application of external selection pressure.
ABSTRACT WORD COUNT: 92
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	514
CLAIMS B	(English)	200127	1730
CLAIMS B	(German)	200127	1667
CLAIMS B	(French)	200127	2184
SPEC A	(English)	EPABF1	8964
SPEC B	(English)	200127	8872
Total word count - document A			9479
Total word count - document B			14453
Total word count - documents A + B			23932

8/3,AB/33 (Item 21 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00468674
Insertion of DNA by modified transposons.
Einfugen von DNS mittels abgewandelter Transposons.
Insertion d'ADN au moyen de transposones modifies.
PATENT ASSIGNEE:
AMERICAN CYANAMID COMPANY, (212591), 1937 West Main Street P.O. Box 60, Stamford Connecticut 06904-0060, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Brey, Robert Newton, III, 74 Sagamore Drive, Rochester, New York 14617, (US)
Deich, Robert Allen, 10 Fallbrook Circle, Rochester, New York 14625, (US)
LEGAL REPRESENTATIVE:
Wachtershauser, Gunter, Dr. (12711), Tal 29, W-8000 Munchen 2, (DE)
PATENT (CC, No, Kind, Date): EP 485701 A1 920520 (Basic)
APPLICATION (CC, No, Date): EP 91114668 910830;
PRIORITY (CC, No, Date): US 590364 900928
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/63; C12N-015/90; A61K-039/00; C12N-015/70; C12N-015/74; C12N-015/30; C12N-015/31
ABSTRACT EP 485701 A1
DNA constructs for the introduction of a DNA sequence into the constituent DNA of a prokaryote, and methods of use. The DNA construct includes an expressible gene encoding a transposase *protein"**, linked in cis to a transposable cassette. The transposable cassete includes a pair of transposase recognition sequences flanking the DNA sequence. The gene encoding the transposase *protein"** is not flanked by the transposase recognition sequences.
ABSTRACT WORD COUNT: 68

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	639
SPEC A	(English)	EPABF1	11212
Total word count - document A			11851
Total word count - document B			0
Total word count - documents A + B			11851

8/3,AB/34 (Item 22 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00446327
VACCINES FOR NONTYPABLE HAEMOPHILUS INFLUENZAE.
IMPFSTOFFE GEGEN HAMOPHILUS INFLUENZAE.
VACCINS CONTRE LES HAEMOPHILUS INFLUENZAE INCLASSIFIABLES.
PATENT ASSIGNEE:
PRAXIS BIOLOGICS, INC., (693521), 30 Corporate Woods, Rochester New York 14623, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;IT;LI;LU;NL;SE)

INVENTOR:
GREEN, Bruce, A., 49 Northfield Gate, Pittsford, NY 14534, (US)
ZLOTNICK, Gary, W., 17 Redwood Drive, Penfield, NY 14526, (US)
LEGAL REPRESENTATIVE:
Allam, Peter Clerk et al (27601), LLOYD WISE, TREGEAR & CO. Norman House 105-109 Strand, London WC2R 0AE, (GB)
PATENT (CC, No, Kind, Date): EP 462210 A1 911227 (Basic)
EP 462210 B1 940907
WO 9010458 900920
APPLICATION (CC, No, Date): EP 90905112 900309; WO 90US1317 900309
PRIORITY (CC, No, Date): US 320971 890309
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/102; C07K-015/04; C12N-015/31; C12N-015/62; C12R-001/21
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	2495
CLAIMS B	(German)	EPBBF1	2364
CLAIMS B	(French)	EPBBF1	2963
SPEC B	(English)	EPBBF1	13186
Total word count - document A			0
Total word count - document B			21008
Total word count - documents A + B			21008

8/3,AB/35 (Item 23 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00397970
*Protein"** anti-cancer agent
*Protein"**-Antikrebsmittel
Agent anticancereux proteique
PATENT ASSIGNEE:
MERCK & CO. INC., (200479), 126, East Lincoln Avenue P.O. Box 2000, Rahway New Jersey 07065-0900, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Oliff, Allen, 1412 Florence Drive, Gwynedd Valley, PA 19401, (US)
Jones, Deborah D., 1126 Canterbury Drive, Lansdale, PA 19446, (US)
Edwards, Gwynneth M., 987 Grange Avenue, Collegeville, PA 19426, (US)
LEGAL REPRESENTATIVE:
Jones, Helen Marjorie Meredith et al (57931), Gill Jennings & Every, Broadgate House, 7 Eldon Street, London EC2M 7LH, (GB)
PATENT (CC, No, Kind, Date): EP 383599 A2 900822 (Basic)
EP 383599 A3 910327
EP 383599 B1 960207
APPLICATION (CC, No, Date): EP 90301639 900215;
PRIORITY (CC, No, Date): US 312540 890217; US 389092 890803; US 449187 891221
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/62; C12N-015/31; C12P-021/02; A61K-047/48; A61K-038/00;

ABSTRACT EP 383599 A2

We have modified PE(sub 4)(sub 0) toxin by removing at least two of its four cysteine amino acid residues and have formed hybrid molecules containing modified PE(sub 4)(sub 0) linked to a cell recognition *protein"** that can be an antibody, a growth factor, a hormone, a lymphokine, or another *polypeptide"** cell recognition *protein"** for which a specific cellular receptor exists whereby the modified PE(sub 4)(sub 0) toxin is directed to cell types having receptors for the cell recognition *protein"** linked to the modified PE(sub 4)(sub 0).
ABSTRACT WORD COUNT: 90

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	426
CLAIMS B	(English)	EPAB96	1001
CLAIMS B	(German)	EPAB96	876
CLAIMS B	(French)	EPAB96	1071
SPEC A	(English)	EPABF1	5533
SPEC B	(English)	EPAB96	5546
Total word count - document A			5959
Total word count - document B			8494
Total word count - documents A + B			14453

8/3,AB/36 (Item 24 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00360221
Covalently-linked complexes and methods for enhanced cytotoxicity and imaging.
Kovalent gebundene Komplexe fur verstarkte Zytotoxizitat und Bildformung.
Complexes covalents et methodes pour cytotoxicite augmentee et pour imagerie.
PATENT ASSIGNEE:
NEORX CORPORATION, (727931), 410 West Harrison Street, Seattle Washington 98119, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Anderson, David C., 2415 Thorndyke Avenue No.301, Seattle Washington 98199, (US)
Morgan, A. Charles, 803 Driftwood Place, Edmonds Washington 98020, (US)
Abrams, Paul G., 2125 First Avenue No.1602, Seattle Washington 98121, (US)
Nichols, Everett J., 12525 17th Avenue N.E., Seattle Washington 98125, (US)
Fritzberg, Alan R., 16703 74th Place West, Edmonds Washington 98020, (US)
LEGAL REPRESENTATIVE:
Wablat, Wolfgang, Dr.Dr. (45393), Potsdamer Chaussee 48, W-1000 Berlin 38 , (DE)
PATENT (CC, No, Kind, Date): EP 359347 A2 900321 (Basic)
EP 359347 A3 900418
EP 359347 B1 921223
APPLICATION (CC, No, Date): EP 89250014 890814;
PRIORITY (CC, No, Date): US 232337 880815
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-047/42; A61K-049/02; A61K-043/00;

ABSTRACT EP 359347 A2
Covalently-linked complexes (CLCs) for targeting a defined population of cells, comprising a targeting *protein"**; a cytotoxic agent; and an enhancing moiety, wherein the enhancing moiety is capable of promoting CLC-target cell interaction are disclosed. Methods for using the claimed CLCs to obtain enhanced in vivo cytotoxicity and enhanced in vivo imaging are also described.
ABSTRACT WORD COUNT: 58

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPABF1	998
SPEC B	(English)	EPABF1	11127
Total word count - document A			0
Total word count - document B			12125
Total word count - documents A + B			12125

8/3,AB/37 (Item 25 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00309467
Methods and compositions for the use of HIV env *polypeptides"** and antibodies thereto
Verfahren und Zubereitungen fur die Verwendung von HIV-env-*Polypeptiden"** und Antikorpern
Methodes et compositions pour l'utilisation de *polypeptides"** env et anticorps anti-env de HIV
PATENT ASSIGNEE:
GENENTECH, INC., (210480), 460 Point San Bruno Boulevard, South San Francisco California 94080, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Berman, Phillip W., 1739 Lexington Avenue, San Mateo, CA 94402, (US)
Gregory, Timothy J., 414 Pinehill Road, Hillsborough, CA 94010, (US)
Lasky, Lawrence A., Star Route Box 40, Sausalito, CA 94965, (US)
Nakamura, Gerald R., 1923, 29th Avenue, San Francisco, CA 94116, (US)
Patzer, Eric J., 470 Tahos Road, Orinda, CA 94563, (US)
Patton, John S., 330 Emerald Avenue, San Carlos, CA 94070, (US)
Vitetta, Ellen S., 6914 Pemberton Drive, Dallas, TX 75230, (US)
LEGAL REPRESENTATIVE:
Stuart, Ian Alexander et al (50492), MEWBURN ELLIS York House 23 Kingsway , London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 279688 A2 880824 (Basic)
EP 279688 A3 890913
EP 279688 B1 970416
APPLICATION (CC, No, Date): EP 88301425 880219;
PRIORITY (CC, No, Date): US 16809 870220; US 57061 870601; US 155336 880212
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-038/00; A61K-039/21; C12P-021/00; A61K-047/00;

ABSTRACT EP 279688 A2
The Human Immunodeficiency Virus envelope *protein"** or its fragments that are capable of binding to the T4 helper lymphocyte receptor are used in therapeutically effective doses for the treatment of

immunoinflammatory disorders or diseases. Amino acid residues that constitue an essential portion of the T4 *receptor"** *binding"** *domain"** of HIV env fall within a 64 residue sequence extending about from residues 411 to 454 of the 3B isolate. This domain is useful as a vaccine component, or for cytotoxic T cell targeting when conjugated with a target cell binding substance. HIV env which is devoid of a functional T4 *receptor"** *binding"** *domain"** is useful as a vaccine for immunization against HIV infection. Antibodies capable of binding this domain also are provided for therapeutic and diagnostic use. An immunotoxin comprising a monoclonal antibody to a virally encoded cell surface antigen, linked to a toxin such as ricin A chain, is disclosed. Also, a method of killing virally infected cells such as HIV infected cells, comprising administering to the infected cells a therapeutically effective amount of the immunotoxin is disclosed.
ABSTRACT WORD COUNT: 182

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	2068
CLAIMS B	(English)	EPAB97	1850
CLAIMS B	(German)	EPAB97	1632
CLAIMS B	(French)	EPAB97	2065
SPEC A	(English)	EPABF1	13054
SPEC B	(English)	EPAB97	12811
Total word count - document A			15123
Total word count - document B			18358
Total word count - documents A + B			33481

8/3,AB/38 (Item 26 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00269301
Combination therapy using anti-tumor monoclonal antibodies and/or immunotoxins with interleukin-2.
Kombinationstherapie mit Verwendung von Antitumor-Monoklonalen Antikorpern und/oder Immunotoxinen mit Interleukin-2.
Therapie combinee utilisant des anticorps anti-tumeurs monoclonaux et/ou des immunotoxines avec l'interleukine-2.
PATENT ASSIGNEE:
CETUS CORPORATION, (229561), 1400 Fifty-Third Street, Emeryville California 94608, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Stevens, Paul, 1126 El Centro Avenue, Oakland California 94602, (US)
Houston, L. L., 1901 Oak Crest Drive, Oakland California 94602, (US)
Zimmerman, Robert, 3912 N. Peardale Drive, Lafayette California 94549, (US)
Koths, Kirston Edward, 2646 Mira Vista Drive, El Cerrito California 94530, (US)
Issell, Brian, 255 Fernwood Drive, Moraga California 94556, (US)
LEGAL REPRESENTATIVE:
Bizley, Richard Edward et al (28352), HEPWORTH, LAWRENCE & BRYER 15th Floor, TerminusHouse Terminus Street, Harlow, Essex CM20 1XD, (GB)
PATENT (CC, No, Kind, Date): EP 256714 A2 880224 (Basic)
EP 256714 A3 891108

APPLICATION (CC, No, Date): EP 87306753 870730;
PRIORITY (CC, No, Date): US 892596 860801; US 55681 870529
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/395; A61K-045/05;

ABSTRACT EP 256714 A2
Anti-tumor activity in humans can be augmented by administering to the mammalian host a pharmacologically effective amount of mammalian IL-2 and at least one immunotoxin that binds selectively to human tumor cells and/or at least one monoclonal antibody that binds selectively to human tumor cells. The IL-2 and immunotoxin and/or antibody are preferably administered separately to the host. The compositions and medications of the invention are useful for prophylactic or therapeutic treatment of such cancers as ovarian and breast cancer.
ABSTRACT WORD COUNT: 84

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	551
SPEC A	(English)	EPABF1	9744
Total word count - document A			10295
Total word count - document B			0
Total word count - documents A + B			10295

8/3,AB/39 (Item 27 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00260239
Recombinant pseudomonas exotoxin: construction of an active immunotoxin with low side effects.
Rekombinantes Pseudomonastoxin : Konstruktion eines wirksamen Immunotoxins mit wenigen Nebenwirkungen.
Exotoxine recombinante de pseudomonas : construction d'une immunotoxine active avec moindres reactions secondaires.
PATENT ASSIGNEE:
Pastan, Ira, (903100), 11710 Beall Mountain Road, Potamac Maryland 20854, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
Fitzgerald, David J., (903110), 1731 Ladd Street, Silver Spring Maryland 20902, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
Adhya, Sankar, (903120), 1440 Kings Grant Street, Gaithersbourg Maryland 20878, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Pastan, Ira, 11710 Beall Mountain Road, Potamac Maryland 20854, (US)
Fitzgerald, David J., 1731 Ladd Street, Silver Spring Maryland 20902, (US)
Adhya, Sankar, 1440 Kings Grant Street, Gaithersbourg Maryland 20878, (US)
LEGAL REPRESENTATIVE:
Patentanwalte Grunecker, Kinkeldey, Stockmair & Partner (100721), Maximilianstrasse 58, D-80538 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 261671 A2 880330 (Basic)
EP 261671 A3 880810

EP 261671 B1 940413
APPLICATION (CC, No, Date): EP 87113929 870923;
PRIORITY (CC, No, Date): US 911227 860924
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-047/48; C07K-015/00;

ABSTRACT EP 261671 A2
Large amounts of various modified forms of Pseudomonas exotoxin are produced. At least one of the modified forms (pJH8) of the exotoxin exhibits low toxicity to human or mouse cells by itself but retains its enzymatic activity and makes a very active cell specific immunotoxin with very low nonspecific cytotoxicity. All the constructs with low cytotoxic activity will be useful as vaccines to produce the antibodies to treat pseudomonas sepsis. In addition, the *protein"** encoded by domain I alone could be administered directly to patients to treat pseudomonas sepsis because that domain would block toxin binding to cells. Clones containing domain II and particularly clone pJH12 can be fused to other toxins which have low activity (such as ricin A chain or pokeweed antiviral *protein"**) to increase their cell-killing activity without increasing their nonspecific binding to cells.
ABSTRACT WORD COUNT: 141

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	2498
CLAIMS B	(German)	EPBBF1	2511
CLAIMS B	(French)	EPBBF1	2906
SPEC B	(English)	EPBBF1	4045
Total word count - document A			0
Total word count - document B			11960
Total word count - documents A + B			11960

8/3,AB/40 (Item 28 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00224489
Anti-human ovarian cancer immunotoxins and methods of use thereof.
Anti-Immuntoxine gegen menschlichen Eierstockkrebs und Verfahren zu deren Verwendung.
Immunotoxines contre le cancer ovarien humain et methodes d'utilisation.
PATENT ASSIGNEE:
CETUS CORPORATION, (229561), 1400 Fifty-Third Street, Emeryville California 94608, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;NL;SE)
THE UNITED STATES OF AMERICA represented by The Secretary The United States Department of Commerce, (301908), , Washington, DC 20230, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;NL;SE)
INVENTOR:
Bjorn, Michael Jon, 109 Olive Court, Hercules California 94547, (US)
Fitzgerald, David, 3319 Lothian Road, Fairfax Virginia 22031, (US)
Frankel, Arthur Edward, 223 Huntington Drive, Chapel N. Carolina 27514, (US)
Laird, Walter Joseph, 2660 Lassen Way, Pinole California 94564, (US)
Pastan, Ira, 11710 Beall Mt. Road, Patomac Maryland 20854, (US)
Ring, David Barratt, 1248 Truman Street, Redwood City California 94061,

(US)
Willingham, Mark, 4301 Chestnut Street, Bethesda Maryland 20814, (US)
Winkelhake, Jeffrey, c/o Cetus Corporation 1400 Fifty-Thirdstreet, Emerville California 94608, (US)
LEGAL REPRESENTATIVE:
Bizley, Richard Edward et al (28352), HEPWORTH LAWRENCE BRYER & BIZLEY 2nd Floor Gate House South West Gate, Harlow, Essex CM20 1JN, (GB)
PATENT (CC, No, Kind, Date): EP 226419 A2 870624 (Basic)
EP 226419 A3 880420
EP 226419 B1 920805
APPLICATION (CC, No, Date): EP 86309516 861205;
PRIORITY (CC, No, Date): US 806320 851206
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: A61K-047/00; A61K-039/395; A61K-037/02;

ABSTRACT EP 226419 A2
Immunotoxins comprising a cytotoxic moiety and monoclonal antibodies which bind to human ovarian cancer tissue having at least one of the following capabilities are claimed: cytotoxic ID(sub 5)(sub 0) of 10 nM or less against human ovarian cancer cells, retardation of human ovarian cancer tumor growth in mammals or extension of survival of a mammal carrying a human ovarian cancer tumor. Antigens to which the monoclonal antibody of the immunotoxin bind are identified and characterize the immunotoxins. Methods of killing human ovarian c
ancer cells, retarding the growth of human ovarian cancer tumors in mammals or extending the survival of mammals carrying human ovarian cancer tumors are claimed.
ABSTRACT WORD COUNT: 159

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	512
CLAIMS B	(German)	EPBBF1	349
CLAIMS B	(French)	EPBBF1	400
SPEC B	(English)	EPBBF1	6604
Total word count - document A			0
Total word count - document B			7865
Total word count - documents A + B			7865

8/3,AB/41 (Item 29 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00224488
Anti-human ovarian cancer immunotoxins and methods of use thereof.
Anti-Immuntoxine gegen menschlichen Eierstockkrebs und Verfahren zu deren Verwendung.
Immunotoxines contre le cancer ovarien humain et methodes d'utilisation.
PATENT ASSIGNEE:
CETUS CORPORATION, (229561), 1400 Fifty-Third Street, Emeryville California 94608, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;NL;SE)
INVENTOR:
Bjorn, Michael Jon, 109 Olive Court, Hercules California 94547, (US)
Frankel, Arthur Edward, 223 Huntington Drive, Chapel North Carolina 27514, (US)

Laird, Walter Joseph, 2660 Lassen Way, Pinole California 94564, (US)
Ring, David Barratt, 1248 Truman Street, Redwood City California 94061, (US)
Winkelhake, Jeffrey Lee, c/o Cetus Corp. 1400 Fifty-Third Street, Emeryville, California 94608, (US)
LEGAL REPRESENTATIVE:
Bizley, Richard Edward et al (28352), HEPWORTH LAWRENCE BRYER & BIZLEY 2nd Floor Gate House South West Gate, Harlow, Essex CM20 1JN, (GB)
PATENT (CC, No, Kind, Date): EP 226418 A2 870624 (Basic)
EP 226418 A3 880427
EP 226418 B1 920527
APPLICATION (CC, No, Date): EP 86309515 861205;
PRIORITY (CC, No, Date): US 806256 851206
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: A61K-047/00; A61K-037/02; A61K-035/74;

ABSTRACT EP 226418 A2

Immunotoxins comprising a cytotoxic moiety and an antigen binding portion selected from the group consisting of Fab, Fab(') and F(ab('))(sub 2) fragments of a monoclonal antibody, which binds to human ovarian cancer tissue, having one of the following capabilities are claimed: cytotoxic ID(sub 5)(sub 0) of about 10 nM or less against human ovarian cancer cells, retardation of human ovarian cancer tumor growth in mammals, or extension of survival of a mammal carrying a human ovarian cancer tumor. Antigens or epitopes to which the monoclonal antibodies bind are identified and characterize the immunotoxins. In a preferred embodiment an immunotoxin comprising at least an antigen binding portion of a monoclonal antibody, which binds to human transferrin receptor, but does not block binding of transferrin to the receptor, is described and claimed. Immunotoxin comprising the (F(ab('))(sub 2) region of the antitransferrin monoclonal antibody are also claimed.

Methods of killing human ovarian cancer cells, retarding the growth of human ovarian tumors in mammals and extending the survival of mammals carrying human ovarian tumors are claimed.
ABSTRACT WORD COUNT: 190

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	922
CLAIMS B	(German)	EPBBF1	484
CLAIMS B	(French)	EPBBF1	566
SPEC B	(English)	EPBBF1	6932
Total word count - document A			0
Total word count - document B			8904
Total word count - documents A + B			8904

8/3,AB/42 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0271346 DBA Accession No.: 2001-10570 PATENT
New *polypeptides"** having *multiple"** *copies"** of a *peptide"** antigen fused to the *receptor"** *binding"** *domain"** of a Pseudomonas exotoxin, useful as a vaccine and for generating antibodies for diagnosis and/or therapeutic procedures - recombinant vaccine

AUTHOR: Hwang J; Hsu C T; Ting C J
CORPORATE SOURCE: Taipei, Taiwan.
PATENT ASSIGNEE: Chinese-Acad.Sci. 2001
PATENT NUMBER: EP 1090994 PATENT DATE: 20010411 WPI ACCESSION NO.: 2001-309780 (2033)
PRIORITY APPLIC. NO.: US 412558 APPLIC. DATE: 19991005
NATIONAL APPLIC. NO.: EP 2000304253 APPLIC. DATE: 20000519
LANGUAGE: English
ABSTRACT: A new *protein"** is claimed. It contains a *receptor"** *binding"** *domain"** of a *Pseudomonas"** *exotoxin"**-*A"** or its functional variant, and at least two copies of a *peptide"** sequence, where, the *peptide"** sequence may also contain a fragment of a vaccine virus coat *protein"** or its functional variant. The *protein"** is produced by providing N1, introducing the DNA into a cell, and expressing the *protein"** in the cell. Also claimed are: a nucleic acid (N1) encoding the *protein"**; a method of producing the *protein"**; and a vaccine composition containing at least one *protein"** or at least nucleic acid and optionally a pharmaceutical carrier. The *protein"** is useful as a vaccine. The *protein"** is useful for generating antibodies that bind a monomeric *peptide"** sequence. Such antibodies are useful in diagnostic or therapeutic procedures that require the enhancement, inhibition or detection of any molecule that contains the epitope presented by the *peptide"**. (15pp)

8/3,AB/43 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0163187 DBA Accession No.: 94-05738 PATENT
Novel receptor-mediated delivery system comprising a cell *receptor"** *binding"** *domain"**, a cytoplasmic translocation domain and a nuclear translocation signal domain - application in Factor-VIII or alpha-1-antitrypsin gene expression for gene therapy
PATENT ASSIGNEE: Miles 1994
PATENT NUMBER: WO 9404696 PATENT DATE: 940303 WPI ACCESSION NO.: 94-083210 (9410)
PRIORITY APPLIC. NO.: US 935074 APPLIC. DATE: 920825
NATIONAL APPLIC. NO.: WO 93US7945 APPLIC. DATE: 930824
LANGUAGE: English
ABSTRACT: A novel composition (I) comprises a *polypeptide"** which contains a *receptor"**-*binding"** *domain"** , a cytoplasmic translocation domain, a nuclear translocation domain and a means for connecting a selected macromolecule to the *polypeptide"**. Also claimed is a method for inserting an exogenous macromolecule into a target cell nucleus, which comprises administering (I) to target cells, incubating the cells and determining transfer by an assay. In (I) the *receptor"** *binding"** *domain"** is preferably a toxin-derived ligand for a specific cell receptor, e.g. diphtheria toxin or *Pseudomonas"** *exotoxin"**-*A"** (PEA). The cytoplasmic translocation domain is derived from PEA. The nuclear translocation signal domain is an SV40 virus, yeast, alpha-2 or a GAL-4 nucleic acid sequence. macromolecule is preferably a nucleotide, oligopeptide, *polypeptic , *protein"** , or nucleic acid encoding Factor-\ alpha-1-antitrypsin, a *polypeptide"** which is a regulator of expression or beta-galactosidase (EC-3.2.1.23). (I) provides a receptor-mediated delivery system which can transport funct macromolecules that will act once internalized into the nucleus.

8/3,AB/44 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0113769 DBA Accession No.: 91-01411
Characterization of hybrid toxins prepared with an exotoxin-A variant deficient in receptor binding - *Pseudomonas"** aeruginosa *exotoxin"** -*A"** *protein"** engineering for reduced cytotoxicity in chimeric toxin (conference abstract)
AUTHOR: Chaudry G J; Fulton R J; Draper R K
CORPORATE SOURCE: Molecular and Cell Biology Program, F03.1, The University of Texas at Dallas, Box 830688, Richardson, Tx 75083, USA.
JOURNAL: J.Cell Biol. (111, 5, Pt.2, 192a) 1990
CODEN: JCLBA3
LANGUAGE: English
ABSTRACT: *Pseudomonas"** aeruginosa *exotoxin"**-*A"** (a cytotoxic *protein"** of mol.wt. 66,583 which activates elongation factor-2 by addition of an adenosine diphosphate ribose moiety of NAD+) comprises a *receptor"** *binding"** *domain"** (domain I), a membrane penetration domain (domain II) and a catalytic domain (domain III). A variant with reduced cytotoxicity has been prepared by genetic engineering to reduce receptor binding. The recombinant toxins may be useful for selective cell killing. A variant designated ETA-60EF61 with Glu-Phe inserted between amino acids 60 and 61 in domain I dissociated from the cell surface rapidly and was 500-fold less cytotoxic than the wild-type toxin. Using this variant, hybrid toxins are being constructed and characterized to assess their potency for selective cell killing. Conjugating ETA-60EF61 to human transferrin produced a hybrid toxin that was significantly more cytotoxic than ETA-60EF61 alone. Receptor binding competition assays using free transferrin demonstrated that the hybrid toxin killed target cells by entering via the transferrin receptor. (0 ref)

Set	Items	Description
S9	34	S1 AND VACCINIA
S10	18	S9 AND (RECEPTOR(1W)DOMAIN? ? OR REPETIT? OR REPEAT? OR MULTIPLE(3N)COPIES)
S11	10	S10 NOT S7
S12	5	RD (unique items)

>>>No matching display code(s) found in file(s): 65, 113

12/3,AB/1 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01337900
Use of p97 and iron binding proteins as diagnostic and therapeutic agents
Verwendung von p97 und Eisenbindungsproteinen als diagnostische und therapeutische Wirkstoffe
Utilisation de p97 et des proteines liant le fer comme agents diagnostiques et therapeutiques
PATENT ASSIGNEE:
UNIVERSITY OF BRITISH COLUMBIA, (2127245), I.R.C. Building, Room 133, Vancouver, British Columbia V6T 1W5, (CA), (Applicant designated States: all)
INVENTOR:

Food, Michael, 2902 A Yew Street, Vancouver, British Columbia V4A 2V5, (CA)
Jefferies, Wilfred A., 12682 Crescent Road, South Surrey, British Columbia V4A 2V5, (CA)
Yamada, Tatsuo, 505, 3-8-2 Akasaka, Chuo-ku, Fukuoka 810-0042, (JP)
Mc Geer, Patrick L., 4727 W 2 Avenue, Vancouver, British Columbia V6T 1C1, (CA)
Rothenberger, Sylvia Dr., Chemin des Planches 45, 1066 Epalinges, (CH)
LEGAL REPRESENTATIVE:
Benedum, Ulrich Max, Dr. et al (72602), Haseltine Lake Partners Motorama Haus 502 Rosenheimer Strasse 30, 81669 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1143253 A1 011010 (Basic)
APPLICATION (CC, No, Date): EP 2001107468 930709;
PRIORITY (CC, No, Date): US 912291 920710
DESIGNATED STATES: DE; FR; GB; IT
RELATED PARENT NUMBER(S) - PN (AN):
EP 651768 (EP 93915585)
INTERNATIONAL PATENT CLASS: G01N-033/68; C12N-005/08

ABSTRACT EP 1143253 A1
The invention relates to a GPI-anchored p97 and a soluble form of p97 and derivatives thereof and methods for identifying a stimulant, agonist or antagonist of p97 as well as for purifying microglial cells associated with Alzheimer's disease (beta)-amyloid plaques. Use of these methods in identifying substances which are effective in the treatment and diagnosis of Alzheimer's disease and for treating conditions involving disturbances in iron metabolism.
ABSTRACT WORD COUNT: 68
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200141	358
SPEC A	(English)	200141	27652
Total word count - document A			28010
Total word count - document B			0
Total word count - documents A + B			28010

12/3,AB/2 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01289147
Polynucleotide encoding autoantigens associated with endometriosis
Endometriose-assoziierte-Autoantigene kodierendes Polynukleotid
Polynucleotide codant pour des auto-antigenes associes a l'endometriose
PATENT ASSIGNEE:
DIAGNOSTIC PRODUCTS CORPORATION, (728210), 5700 West 96th Street, Los Angeles California 90045, (US), (Applicant designated States: all)
INVENTOR:
El Shami, A. Said, 11016 Red Barn Road, Camarillo, California 93032, (US)
Menon, Surendra Nath, 4052 Jackson Avenue, Culver City, California 90232, (US)
French, Cynthia K., 14 Virgil Court, Irvine, California 92612, (US)
LEGAL REPRESENTATIVE:

Campbell, Patrick John Henry et al (80141), J.A. Kemp & Co., 14 South Square, Gray's Inn, London WC1R 5JJ, (GB)
PATENT (CC, No, Kind, Date): EP 1106690 A2 010613 (Basic)
EP 1106690 A3 010725
APPLICATION (CC, No, Date): EP 2000310408 001123;
PRIORITY (CC, No, Date): US 447399 991123
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12N-015/12; C07K-014/47; C12Q-001/68; C12N-005/10; C07K-016/18; G01N-033/53; G01N-033/557; C07K-019/00; A61K-038/17

ABSTRACT EP 1106690 A3
This invention provides a polynucleotide encoding Repro-EN-1.0 and IB1, polypeptides associated with endometriosis. Auto-antibodies against Repro-EN-1.0 and IB1 have been found in subjects diagnosed with endometriosis. This invention also provides methods of using this polynucleotide and polypeptide.
ABSTRACT WORD COUNT: 38
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200124	2421
SPEC A	(English)	200124	20110
Total word count - document A			22531
Total word count - document B			0
Total word count - documents A + B			22531

12/3,AB/3 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00743293
COMPOSITIONS AND METHODS FOR TARGETING GENE DELIVERY VEHICLES
VERFAHREN UND ZUSAMMENSETZUNGEN ALS VEHIKEL ZUR ZIELGERICHTETE EINBRINGEN VON GENEN
COMPOSITIONS ET PROCEDES DE CRIBLAGE DE VECTEURS D'APPORT DE GENES
PATENT ASSIGNEE:
CHIRON CORPORATION, (572530), 4560 Horton Street, Emeryville, California 94608, (US), (Proprietor designated states: all)
INVENTOR:
JOLLY, Douglas, J., 277 Hillcrest Drive, Leucadia, CA 92024, (US)
BARBER, Jack, R., 11168 Carlotta Street, San Diego, CA 92129, (US)
RESPESS, James, G., 4966 Lamont Street, San Diego, CA 92109, (US)
MOORE, Margaret, Dow, 3616 Jennifer Street, San Diego, CA 92117, (US)
LEGAL REPRESENTATIVE:
Goldin, Douglas Michael et al (31061), J.A. KEMP & CO. 14 South Square Gray's Inn, London WC1R 5LX, (GB)
PATENT (CC, No, Kind, Date): EP 759087 A1 970226 (Basic)
EP 759087 B1 010328
WO 9531566 951123
APPLICATION (CC, No, Date): EP 95920449 950515; WO 95US6084 950515
PRIORITY (CC, No, Date): US 242407 940513

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/86; A61K-048/00
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200113	1535
CLAIMS B	(German)	200113	1393
CLAIMS B	(French)	200113	1755
SPEC B	(English)	200113	18153
Total word count - document A			0
Total word count - document B			22836
Total word count - documents A + B			22836

12/3,AB/4 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00615029
USE OF p97 IN THE DIAGNOSIS OF ALZHEIMER DISEASE
VERWENDUNG VON P97 IN DER DIAGNOSE VON MORBUS ALZHEIMER
UTILISATION DE p97 POUR LE DIAGNOSTIQUE DE LA MALADIE ALZHEIMER
PATENT ASSIGNEE:
UNIVERSITY OF BRITISH COLUMBIA, (917321), Room 331, IRC Building, 2194 Health Sciences Mall, Vancouver, British Columbia, V6T 1Z3, (CA), (Proprietor designated states: all)
INVENTOR:
JEFFERIES, Wilfred, A., 12682 Crescent Road, South Surrey, British Columbia V4A 2V5, (CA)
McGEER, Patrick, L., 4727 W 2 Avenue, Vancouver, British Columbia V6T 1C1 , (CA)
ROTHENBERGER, Sylvia, Grand Chemin 59, 1066 Epalinges, (CH)
FOOD, Michael, R., 3149 West 7th Avenue, Vancouver, British Columbia V6K 1Z9, (CA)
YAMADA, Tatsuo, 4-2-16-203 Sannou Ohta-Ku, Tokyo, (JP)
LEGAL REPRESENTATIVE:
Sunderland, James Harry (47953), HASELTINE LAKE PARTNERS Motorama Haus 502 Rosenheimer Strasse 30, 81669 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 651768 A1 950510 (Basic)
EP 651768 B1 011107
WO 9401463 940120
APPLICATION (CC, No, Date): EP 93915585 930709; WO 93CA272 930709
PRIORITY (CC, No, Date): US 912291 920710
DESIGNATED STATES: DE; FR; GB; IT
RELATED DIVISIONAL NUMBER(S) - PN (AN):
EP 1018343 (EP 2000101634)
EP 1143253 (EP 2001107468)
INTERNATIONAL PATENT CLASS: C07K-014/435; C07K-014/705; G01N-033/08; C12N-005/02; A61K-038/17
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200145	224

CLAIMS B	(German)	200145	207
CLAIMS B	(French)	200145	258
SPEC B	(English)	200145	26633
Total word count - document A			0
Total word count - document B			27322
Total word count - documents A + B			27322

12/3,AB/5 (Item 5 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00517411
Monoclonal antibody, polypeptides and production thereof
Monoklonaler Antikorper, Polypeptide und deren Herstellung
Anticorps monoclonal, polypeptides et leur production
PATENT ASSIGNEE:
TAKEDA CHEMICAL INDUSTRIES, LTD., (204706), 1-1, Doshomachi 4-chome, Chuo-ku, Osaka 541, (JP), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;PT;SE)
Miyake, Masayuki, (1490970), 76, Daigo-ohatacho, Fushimi-ku, Kyoto 601-13, (JP), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;PT;SE)
INVENTOR:
Ikeyama, Shuichi, 32-15 Nanpeidai 5-chome, Takatsuki, Osaka 569, (JP)
Koyama, Masaru, A-207, 1 Satsukigaokanishi, Suita, Osaka 565, (JP)
Senoo, Masaharu, 10-13, Kadotabunkacho 2-chome, Okayama 700, (JP)
Miyake, Masayuki, 76, Daigo-ohatacho, Fushimi-ku, Kyoto 601-13, (JP)
LEGAL REPRESENTATIVE:
von Kreisler, Alek, Dipl.-Chem. et al (12434), Patentanwalte von Kreisler-Selting-Werner Postfach 10 22 41, 50462 Koln, (DE)
PATENT (CC, No, Kind, Date): EP 508417 A2 921014 (Basic)
EP 508417 A3 930512
EP 508417 B1 990714
APPLICATION (CC, No, Date): EP 92106093 920409;
PRIORITY (CC, No, Date): JP 7999691 910412; JP 8539691 910417; JP 2232192 920207
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12P-021/08; C12N-015/12; C07K-014/435; A61K-039/395; A61K-038/17; C07K-016/30;

ABSTRACT EP 508417 A2
The present invention relates to a monclonal antibody capable of suppressing the motility of cancer cells, a polypeptide recognizable by said anti-cancer antibody and its fragment peptides which is capable of suppressing the motility of cancer cells.
The present invention also relates to a production and a use for preventing the metastasis of cancer thereof.
ABSTRACT WORD COUNT: 57

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9928	224
CLAIMS B	(German)	9928	192
CLAIMS B	(French)	9928	268
SPEC B	(English)	9928	9578

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Total word count - document A            0
Total word count - document B        10262
Total word count - documents A + B   10262

Set     Items   Description
S13      4617   AU=(HWANG, J? OR HWANG J?)
S14      6559   AU=(HSU, C? OR HSU C?)
S15      1152   AU=(TING, C? OR TING C?)
S16        10   S13 AND S14 AND S15
S17        52   S13 AND (S14 OR S15)
S18        18   S14 AND S15
S19     12258   S13 OR S14 OR S15
S20        29   S19 AND (S2 OR S9)
S21        75   (S16 OR S17 OR S18 OR S20) NOT (S7 OR S11)
S22        18   RD (unique items)
>>>No matching display code(s) found in file(s): 65, 113
```

- Author(s)

```
 22/3,AB/1     (Item 1 from file: 65)
DIALOG(R)File  65:Inside Conferences
(c) 2001 BLDSC all rts. reserv. All rts. reserv.

03385202   INSIDE CONFERENCE ITEM ID: CN035747102
A Study on the Shallow Water Wave Equation with the Presence of  Currents
  Lin, M. C.; *Hsu, C. M."**; *Ting, C. L."**
  CONFERENCE: International offshore and polar engineering conference-10th
  PROCEEDINGS OF THE INTERNATIONAL OFFSHORE AND POLAR ENGINEERING
  CONFERENCE, 2000; 10TH; VOLUME 3  P: 647-654
  International Society of Offshore and Polar Engineers, 2000
  ISSN: 1098-6189 ISBN: 188065346X; 1880653494
  LANGUAGE: English  DOCUMENT TYPE: Conference Papers
    CONFERENCE EDITOR(S): Chung, J. S.
    CONFERENCE SPONSOR: International Society of Offshore and Polar
          Engineers
    CONFERENCE LOCATION: Seattle, WA
    CONFERENCE DATE:  May 2000
  NOTE:
    See also same shelfmark in V-Store for papers held on CD-ROM


 22/3,AB/2     (Item 2 from file: 65)
DIALOG(R)File  65:Inside Conferences
(c) 2001 BLDSC all rts. reserv. All rts. reserv.

02851121   INSIDE CONFERENCE ITEM ID: CN029743366
A New 8 Pin Power Factor Correction and Pulse Width Modulator  Controller
for Off-Line Power Supplies
  *Hwang, J."**; *Hsu, C."**
  CONFERENCE: Annual applied power electronics conference-14th
  APEC -IEEE-, 1999; CONF 14; VOL 2  P: 1143-1149
  IEEE Operations Center, 1999
  ISBN: 0780351614; 0780351606; 0780351622; 0780351630
  LANGUAGE: English  DOCUMENT TYPE: Conference Papers and programme
    CONFERENCE SPONSOR: IEEE
    CONFERENCE LOCATION: Dallas, TX
    CONFERENCE DATE:  Mar 1999 (199903) (199903)
  NOTE:
    IEEE cat no 99CH36285, 99CB36285 and 99CH36285C
```

22/3,AB/3 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

14630773 PASCAL No.: 00-0301421
Development of DNA delivery system using *Pseudomonas"** *exotoxin"** *A"** and a DNA binding region of human DNA topoisomerase I
CHEN T Y; *HSU C T"**; CHANG K H; *TING C Y"**; WHANG-PENG J; HUI C F; *HWANG J"**
Institute of Genetics, School of Life Science, National Yang-Ming University, Nankang, Taipei, Taiwan; Institute of Zoology, Academia Sinica, Nankang, Taipei, 115, Taiwan; Institute of Molecular Biology, Academia Sinica, Nankang, Taipei, Taiwan, ROC, Taiwan; Clinical Research Center, National Health Research Institutes, Nankang, Taipei, Taiwan
Journal: Applied microbiology and biotechnology, 2000, 53 (5) 558-567
Language: English
Gene therapy is defined as the delivery of a functional gene for expression in somatic tissues with the intent to cure a disease. Thus, highly efficient gene transfer is essential for gene therapy. Receptor-mediated gene delivery can offer high efficiency in gene transfer, but several technical difficulties need to be solved. In this study, we first examined the DNA binding regions of the human DNA topoisomerase I (Topo I), using agarose gel mobility shift assay, in order to identify sites of noncovalent binding of human DNA Topo I to plasmid DNA. We identified four DNA binding regions in human DNA Topo I. They resided in aa 51-200, 271-375, 422-596. and 651-696 of the human DNA Topo I. We then used one of the four regions as a DNA binding *protein"** fragment in the construction of a DNA delivery vehicle. Based on the known functional property of each *Pseudomonas"** *exotoxin"** *A"** (PE) domain and human DNA Topo I, we fused the receptor binding and membrane translocation domains of PE with a highly positively charged DNA binding region of the N-terminal 198 amino acid residues of human DNA Topo I. The resulting recombinant *protein"** was examined for DNA binding in vitro and transfer efficiency in cultured cells. The results show that this DNA delivery *protein"** is a general DNA delivery vehicle without DNA sequence, topology, and cell-type specificity. The DNA delivery *protein"** could be used to target genes of interest into cells for genetic and biochemical studies. Therefore, this technique can potentially be applied to cancer gene therapy.

22/3,AB/4 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

14321645 PASCAL No.: 99-0529475
Recombinant *protein"** composed of *Pseudomonas"** *exotoxin"** *A"**, outer membrane *proteins"** I and F as vaccine against P. aeruginosa infection
CHEN T Y; SHANG H F; CHEN T L; LIN C P; HUI C F; *HWANG J"**
Institute of Genetics, School of Life Sciences, National Yang-Ming University, Taipei, 115, Taiwan; Institute of Molecular Biology, Academia Sinica, Nankang, Taipei, 115, Taiwan; Department of Microbiology, Taipei Medical College, Taipei, Taiwan; Institute of Zoology, Academia Sinica, Nankang, Taipei, 115, Taiwan; Division of Drug Biology, National

Laboratories of Foods and Drugs, Department of Health, Taipei, Taiwan
Journal: Applied microbiology and biotechnology, 1999, 52 (4) 524-533
Language: English

We have constructed a chimeric *protein"** composed of the receptor binding and membrane translocation domains of *Pseudomonas"** *exotoxin"** *A"** (PE) with the outer membrane *proteins"** I and F, together designated as PEIF. The potential of PEIF as a vaccine against Pseudomonas infection was evaluated in BALB/c mice and New Zealand white rabbits. We examined titers of anti-PE and anti-OprF antibodies, and the ability both to neutralize PE cytotoxicity and to increase opsonophagocytic uptake of Pseudomonas aeruginosa strain PAO1, serogroups 2 and 6. The results showed that PEIF can induce antibodies not only to neutralize the PE cytotoxicity but also to promote the uptake of various strains of P. aeruginosa by murine peritoneal macrophages. In a burned mouse model, PEIF afforded significant protection against infection by the homologous P. aeruginosa strain PAO1, heterologe Institute
of Technology, Taoyuan, 320, Taiwan; Department of Chemical Engineering, National Chung Hsing University, Taichung, 400, ROC, Taiwan
Journal: Polymer : (Guildford), 1998, 39 (26) 6911-6920
Language: English

A series of copolymethacrylates with different contents of tolane-based mesogenic groups have been synthesized. The mesogenic group content was characterized with 'H n.m.r. The phase behaviours were determined using a differential scanning calorimeter and optical polarizing microscopy. A smectic A phase was obtained when the mesogenic group content was increased up to 80 mol.%. Dielectric relaxation results indicated that the amplitude of the alpha -relaxation was suppressed significantly due to the presence of the liquid crystalline phase. The reduction of the molecular motion is beneficial to the enhancement of the temporal stability of the effective second-harmonic coefficient for the polymer with a higher mesogenic group content. Moreover, the second harmonic coefficient is enhanced as the mesogenic group content increases. The self-alignment nature of the liquid crystal phase is favourable for alignment of the NLO-active mesogenic group under an applied electric field and preserving such alignment after removal of the electric field. The relationship between thermal dynamic behaviour and second-order nonlinear optical properties is also discussed.

22/3,AB/6 (Item 4 from file: 144)
DIALOG(R)File 144:Pascal

12993587 PASCAL No.: 97-0273495
Identification of mutations at DNA topoisomerase I responsible for camptothecin resistance
WANG L F; *TING C Y"**; LO C K; SU J S; MICKLEY L A; FOJO A T; WHANG-PENG J; *HWANG J"**
Institute of Molecular Biology, Academia Sinica, Nankang, Taiwan; Department of Biochemistry, Taipei Medical College, Taipei, 11529, Taiwan; Medicine Branch, National Cancer Institute, NIH, Bethesda, Maryland 20892, United States; Institute of Biomedical Sciences, Academia Sinica, Nankang, Taiwan
Journal: Cancer research : (Baltimore), 1997, 57 (8) 1516-1522
Language: English

A camptothecin-resistant cell line that exhibits more than 600-fold resistance to camptothecin, designated CPT SUP R -2000, was established

from mutagen-treated A2780 ovarian cancer cells. CPT SUP R -2000 cells also exhibit 3-fold resistance to a DNA minor groove-binding ligand Ho33342, a different class of mammalian DNA topoisomerase I inhibitors. However, CPT SUP R -2000 cells exhibit no cross-resistance toward drugs such as Adriamycin, amsacrine, vinblastine, and 4'-dimethyl-epipodophyllotoxin. The mRNA, protein levels, and enzyme-specific activity of DNA topoisomerase I are relatively the same in parental and CPT SUP R -2000 cells. However, unlike the DNA topoisomerase I activity of parental cells, which can be inhibited by camptothecin, that of CPT SUP R -2000 cells cannot. In addition, parental cells after camptothecin treatment results in a decrease in the level of DNA topoisomerase I, whereas CPT SUP R -2000 cells are insensitive to camptothecin treatment. These results suggested that the mechanism of camptothecin resistance is most likely due to a DNA topoisomerase I structural mutation. This notion is supported by DNA sequencing results confirming that DNA topoisomerase I of CPT SUP R -2000 is mutated at amino acid residues Gly SUP 7 SUP 1 SUP 7 to Val and Thr SUP 7 SUP 2 SUP 9 to Ile. We also used the yeast system to examine the mutation(s) responsible for camptothecin resistance. Our results show that each single amino acid change results in partial resistance, and the double mutation gives a synergetic effect on camptothecin resistance. Because both mutation sites are near the catalytic active center, this observation raises the possibility that camptothecin may act at the vicinity of the catalytic active site of the enzyme-camptothecin-DNA complex.

22/3,AB/7 (Item 5 from file: 144)
DIALOG(R)File 144:Pascal

12220953 PASCAL No.: 95-0440039
A target-specific chimeric toxin composed of epidermal growth factor and *Pseudomonas"** *exotoxin"** *A"** with a deletion in its toxin-binding domain
LIAO C W; HSEU T H; *HWANG J"**
Acad. sinica, inst. molecular biology, Taipei 11529, Taiwan
Journal: Applied microbiology and biotechnology, 1995, 43 (3) 498-507
Language: English
We have fused the epidermal growth factor (EGF) to the amino terminus of *Pseudomonas"** *exotoxin"** *A"** (PE) to create a cytotoxic agent, designated EGF-PE, which preferentially kills EGF-receptor-bearing cells. In this study, we analyzed the effect of the Ia domain, the binding domain, of PE on the cytotoxicity of EGF-PE towards EGF-receptor-bearing cells and tried to develop a more potent EGF-receptor-targeting toxin. EGF-PE molecules with sequential deletions at the amino terminus of PE were constructed and expressed in E. coli strain BL21(DE3). The cytotoxicity of these chimeric toxins was then examined. Our results show that the amino-terminal and carboxy-terminal regions of the Ia domain of PE are important for the cytotoxicity of a PE-based targeting toxin. To design a more potent PE-based EGF-receptor-targeting toxin, a chimeric toxin, named EGF-PE (A34-220), which had most of the Ia domain deleted but retained amino acid residues 1-33 and 221-252 of this domain, was constructed. EGF-PE(DELTA 34-220) has EGF-receptor-binding activity but does not show PE-receptor-binding activity and is mildly cytotoxic to EGF-receptor-deficient NR6 cells. As expected, EGF-PE(DELTA 34-220) is a more potent cytotoxic agent towards EGF-receptor-bearing cells than EGF-PE(DELTA 1-252), where the entire Ia domain of PE was deleted. In addition,

EGF-PE(534-220) was shown to be extremely cytotoxic to EGF-receptor-bearing cancer cells, such as A431,

22/3,AB/8 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

13203572 GENUINE ARTICLE#: 488FM NUMBER OF REFERENCES: 58
TITLE: 26 S proteasome-mediated degradation of topoisomerase II cleavable complexes
AUTHOR(S): Mao Y; Desai SD; *Ting CY"**; *Hwang JL"**; Liu LF (REPRINT)
AUTHOR(S) E-MAIL: lliu@umdnj.edu
CORPORATE SOURCE: Univ Med & Dent New Jersey, Dept Pharmacol, 675 Hoes Ln/Piscataway//NJ/08854 (REPRINT); Univ Med & Dent New Jersey, Dept Pharmacol, /Piscataway//NJ/08854; Acad Sinica, Inst Mol Biol, /Taipei 115//Taiwan/
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF BIOLOGICAL CHEMISTRY, 2001, V276, N44 (NOV 2), P 40652-40658
PUBLISHER: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA
ISSN: 0021-9258
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: DNA topoisomerase II (TOP2) cleavable complexes represent an unusual type of DNA damage characterized by reversible TOP2-DNA cross-links and DNA double strand breaks. Many antitumor drugs and physiological stresses are known to induce TOP2 cleavable complexes leading to apoptotic cell death and genomic instability. However, the molecular mechanism(s) for repair of TOP2 cleavable complexes remains unclear. In the current studies, we show that TOP2 cleavable complexes induced by the prototypic TOP2 poison VM-26 are proteolytically degraded by the ubiquitin/26 S proteasome pathway. Surprisingly the TOP2 beta isozyme is preferentially degraded over TOP2 alpha isozyme. In addition, transcription inhibitors such as 5,6-dichlorobenzimidazole riboside and camptothecin can substantially block VM-26-induced TOP2 beta degradation. These results are consistent with a model in which the repair of TOP2 beta cleavable complexes may involve transcription-dependent proteolysis of TOP2 beta to reveal the protein-concealed double strand breaks.

22/3,AB/9 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

13164078 GENUINE ARTICLE#: 484EL NUMBER OF REFERENCES: 17
TITLE: Photoluminescence and electroluminescence characteristics of new disubstituted polyacetylenes
AUTHOR(S): *Ting CH"**; *Hsu CS (REPRINT)"**
CORPORATE SOURCE: Natl Chiao Tung Univ, Dept Appl Chem, /Hsinchu 30050//Taiwan/ (REPRINT); Natl Chiao Tung Univ, Dept Appl Chem, /Hsinchu 30050//Taiwan/
PUBLICATION TYPE: JOURNAL
PUBLICATION: JAPANESE JOURNAL OF APPLIED PHYSICS PART 1-REGULAR PAPERS SHORT NOTES & REVIEW PAPERS, 2001, V40, N9A (SEP), P5342-5345
PUBLISHER: INST PURE APPLIED PHYSICS, DAINI TOYOKAIJI BLDG, 4-24-8 SHINBASHI, MINATO-KU TOKYO, 105-004, JAPAN

ISSN: 0021-4922
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: Three di-substituted acetylenes in the tolane structure, 4-(trans-4-pentylcyclohexyl)-3',4'-difluorotolane (1M), 4-(trans-4-heptylcyclohexyl)-4'-fluorotolane (2M), and 4-(4-pentylphenyl)-4'-fluorotolane (3M), were polymerized in the presence of TaCl5-based catalyst. The weight-average molecular weights Mw of the polymers were high than 4 x 10(5). Photoluminescence (PL) and electroluminescence (EL) of the three polymers made as single-layer device on indium-tin oxide glass (ITO), ITO/polymer/Al, have been comprehensively studied. By changing the structural conditions of polymer, such as introducing the fluorine atom or a long carbon chain to the end group of polymer side chains, the luminescence is clearly enhanced.

22/3,AB/10 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

13146660 GENUINE ARTICLE#: 480KC NUMBER OF REFERENCES: 26
TITLE: Synthesis and photoluminescence property of polyacetylenes containing liquid crystalline side groups
AUTHOR(S): *Ting CH"**; *Hsu CS (REPRINT)"**
AUTHOR(S) E-MAIL: cshsu@cc.nctu.edu.tw
CORPORATE SOURCE: Natl Chiao Tung Univ, Dept Appl Chem, /Hsinchu 300//Taiwan/ (REPRINT); Natl Chiao Tung Univ, Dept Appl Chem, /Hsinchu 300//Taiwan/
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF POLYMER RESEARCH-TAIWAN, 2001, V8, N3 (SEP), P 159-167
PUBLISHER: POLYMER SOC, TAIPEI, NATL TSING HUA UNIV, CHEMICAL ENG DEPT,, HSINCHU 30043, TAIWAN
ISSN: 1022-9760
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: A series of new side-chain liquid crystalline (LC) polyacetylenes containing 4-(trans-n-alkyleyclohexanylcarbonyloxy)phenyl 4-alkynyloxybenzoate side groups were synthesized by using [Rh(nbd)Cl](2), WCl6 and MoCl5 as polymerization catalysts. The synthesized polymers were characterized by differential scanning calorimetry, optical microscopy and X-ray diffraction measurements. The monomers showed a nematic phase while all polymers revealed the nematic, smectic A and smectic C phases. X-ray diffraction measurements proved that all the polymers show an interdigitated bilayer structure. The optical properties of the polymers were investigated by UV-vis and photoluminescent spectroscopies. The polymer films emitted green-blue photoluminescence at about 500 nm.

22/3,AB/11 (Item 4 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

10906310 GENUINE ARTICLE#: 234GB NUMBER OF REFERENCES: 41
TITLE: A nontoxic *Pseudomonas"** *exotoxin"** *A"** induces active immunity and passive protective antibody against *Pseudomonas"** *exotoxin"** *A"** intoxication
AUTHOR(S): Chen TY; Lin CP; Loa CC; Chen TL; Shang HF; *Hwang

JL (REPRINT)"**; Hui CF
AUTHOR(S) E-MAIL: jh@ccvax.sinica.edu.tw
CORPORATE SOURCE: Acad Sinica, Inst Mol Biol, /Taipei 115//Taiwan/ (REPRINT); Acad Sinica, Inst Mol Biol, /Taipei 115//Taiwan/; Natl Yang Ming Univ, Inst Genet, /Taipei 112//Taiwan/; Natl Labs Foods & Drugs, Div Drug Biol, /Taipei//Taiwan/; Soochow Univ, Grad Sch Microbiol, /Taipei//Taiwan/; Taipei Med Coll, Dept Med, /Taipei//Taiwan/; Acad Sinica, Inst Zool, /Taipei//Taiwan/
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF BIOMEDICAL SCIENCE, 1999, V6, N5 (SEP-OCT), P 357-363
PUBLISHER: KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND
ISSN: 1021-7770
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: *Pseudomonas"** *exotoxin"** *A"** (PE) is one of the most potent cytotoxic agents produced by Pseudomonas aeruginosa. In this study, we examined the possibility of using PE with a deletion of 38 carboxyl-terminal amino acid residues, designated PE(Delta 576-613), for active immunization against PE-mediated disease. We first examined the toxic effects of PE and PE(Delta 576-613) on 5- and 9-week-old ICR mice, The results show that the subcutaneous administration of PE(Delta 576-613) at a dose of 250 mu g was still nontoxic to 5- and 9-week-old ICR mice, while native PE was lethal at a dose of 0.5 and 1 mu g, respectively. PE(Delta 576-613) was then used to immunize ICR mice. The minimum dose of PE(Delta 576-613) that could effectively induce anti-PE antibodies in 5- and 9-week-old ICR mice was found to be 250 ng, However, immunization with 250 ng PE(Delta 576-673) failed to protect the immunized mice from a lethal dose of PE, The effective immunization dose of PE(Delta 576-613) that could protect mice against a 2 mu g PE challenge was found to be 15 Gig. In addition, sera obtained from PE(Delta 576-613)-immunized ICR mice were able to neutralize PE intoxication and effectively protect mice from PE, Thus, PE(Delta 576-613) may be used as an alternative route to new PE vaccine development.

22/3,AB/12 (Item 5 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

07872224 GENUINE ARTICLE#: VQ351 NUMBER OF REFERENCES: 29
TITLE: Characterization of monoclonal antibody B7, which neutralizes the cytotoxicity of *Pseudomonas"** aeruginosa *exotoxin"** *A"**
AUTHOR(S): Shang HF; Yeh ML; Lin CP; *Hwang JL"**
CORPORATE SOURCE: ACAD SINICA,INST MOL BIOL/TAIPEI 11529//TAIWAN/ (REPRINT) ; ACAD SINICA,INST MOL BIOL/TAIPEI 11529//TAIWAN/; NATL YANG MING UNIV,INST MICROBIOL & IMMUNOL/TAIPEI 112//TAIWAN/; TAIPEI MED COLL,DEPT MICROBIOL/TAIPEI//TAIWAN/; NATL LABS FOODS & DRUGS,DIV DRUG BIOL, DEPT HLTH/TAIPEI//TAIWAN/
PUBLICATION TYPE: JOURNAL
PUBLICATION: CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, 1996, V3, N6 (NOV), P727-732
PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171
ISSN: 1071-412X
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: A nontoxic *Pseudomonas"** aeruginosa *exotoxin"** *A"** (PE), which has the carboxyl-terminal 38 amino acid residues of native PE

deleted, was used as an antigen to immunize BALB/c mice, which were then challenged with native PE in order to raise monoclonal antibodies (MAbs) that can neutralize PE cytotoxicity. A murine MAb against PE, designated MAb B7, was established, MAb B7 was characterized in terms of its ability to neutralize PE cytotoxicity, epitope mapping, inhibition of PE receptor binding, and influence on cellular processing of PE and ADP-ribosylation activities, We found that MAb B7 could neutralize PE cytotoxicity in cell culture and in BALB/c mice, The epitope recognized by MAb B7 was mapped to the carboxyl-terminal amino acid residues575 to 595 of PE. Consistent with the results of epitope mapping, MAb B7 did not block PE receptor-binding activity or the cellular processing of PE but strongly inhibited the ADP-ribosylating activity of PE, In addition, MAb B7 retained strong binding to PE even at pH 4.0, indicating that the complex of MAb B7 and PE is stable in the phagolysosome. On the basis of these observations, the neutralization of PE cytotoxicity by MAb B7 could be due to its binding to the carboxyl terminus of PE, As a result, MAb B7 may interfere with the interaction of the carboxyl-end amino acid residues REDLK ofPE with cellular factors, However, we could not rule out the possibility that MAb B7 directly blocks the ADP-ribosylation activity of PE in the cytosol.

22/3,AB/13 (Item 6 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

04633204 GENUINE ARTICLE#: LG328 NUMBER OF REFERENCES: 48
TITLE: AN EGF-*PSEUDOMONAS"** *EXOTOXIN"**-*A"** RECOMBINANT *PROTEIN"** WITH A DELETION IN TOXIN BINDING DOMAIN SPECIFICALLY KILLS EGF RECEPTOR BEARING CELLS
AUTHOR(S): LEE CH; LEE EC; TSAI ST; KUNG HJ; LIU YC; *HWANG JL (Reprint)"**
CORPORATE SOURCE: CHINESE ACAD SCI,INST MOLEC BIOL/BEIJING//PEOPLES R CHINA/ (Reprint); CHINESE ACAD SCI,INST MOLEC BIOL/BEIJING//PEOPLES R CHINA/; CASE WESTERN RESERVE UNIV,SCH MED,DEPT MOLEC BIOL & MICROBIOL/CLEVELAND//OH/44106; NATL TSING HUA UNIV,INST LIFE SCI/HSINCHU 300//TAIWAN/; VET GEN HOSP,CLIN RES CTR/TAIPEI//TAIWAN/
PUBLICATION: PROTEIN ENGINEERING, 1993, V6, N4 (JUN), P433-440
ISSN: 0269-2139
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE
ABSTRACT: We constructed two chimeric toxins; one composed of epidermal growth factor (EGF) and *pseudomonas"** *exotoxin"** *A"** (PE), designated EGF-PE and the other composed of EGF and PE with a deletion of the 1a domain (cell-binding domain), designated EGF-PE (DELTAIa). Both chimeric toxins reacted with anti-EGF and anti-PE antibodies. The cell-killing experiments showed that EGF-PE, but not EGF-PE(DELTAIa), was cytotoxic to the murine fibroblast cell line NR6, which carried the PE receptor, but not the EGF receptor. However, after NR6 was transfected with DNA for the expression of human EGF receptor, the transfected cell line, designated NRHER5, over-expressed h receptors and became sensitive to EGF-PE(DELTAIA). The cyt EGF-PE(DELTAIa), but not EGF-PE, to NRHER5 can be complete an excess amount of EGF. To completely reverse the cytotox EGF-PE on NRHER5, both the EGF receptor pathway and the PE pathway need to be blocked. These results suggest that EGF both EGF and PE binding activities, while EGF-PE(DELTAIA) only EGF binding activity. Thus, EGF-PE(DELTAIa) may be a chimeric toxin than EGF-PE in terms of target specificity t

receptor bearing cells. We, therefore, examined the cytotoxicity of EGF-PE(DELTAIa) to various human cancer cell tines. We find that human cancer cells containing more EGF receptors are more sensitive to EGF-PE(DELTAIa).

22/3,AB/14 (Item 7 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

04147608 GENUINE ARTICLE#: JZ239 NUMBER OF REFERENCES: 45
TITLE: *PSEUDOMONAS"** *EXOTOXIN"** *A"**-EPIDERMAL GROWTH FACTOR (EGF) MUTANT CHIMERIC *PROTEIN"** AS AN INDICATOR FOR IDENTIFYING AMINO ACID RESIDUES IMPORTANT IN EGF-RECEPTOR INTERACTION
AUTHOR(S): SHIAH HS; CHEN TY; CHANG CM; CHOW JT; KUNG HJ; *HWANG JL (Reprint)"**
CORPORATE SOURCE: ACAD SINICA,INST MOLEC BIOL/TAIPEI 11529//TAIWAN/ (Reprint); ACAD SINICA,INST MOLEC BIOL/TAIPEI 11529//TAIWAN/; CASE WESTERN RESERVE UNIV,SCH MED,DEPT MOLEC BIOL & MICROBIOL/CLEVELAND//OH/44106
PUBLICATION: JOURNAL OF BIOLOGICAL CHEMISTRY, 1992, V267, N33 (NOV 25), P 24034-24040
ISSN: 0021-9258
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE
ABSTRACT: Epidermal growth factor (EGF) was fused to the carboxyl end of a modified *pseudomonas"** *exotoxin"** *A"** that has its toxin binding domain deleted. This chimeric toxin designated as PE(DELTAIa)-EGF kills A431 cells through the EGF receptor-mediated pathway. In this study, we used a random mutagenesis approach to make point mutations on EGF, followed by replacing the wild type EGF in PE(DELTAIa)-EGF with these EGF mutants. We have constructed 14 different PE(DELTAIa)-EGF(mutants), and examined their EGF receptor binding activity as well as their cytotoxicity to A431 cells. Our results showed that individual mutations of Val19 to Glu and Val34 to Asp in the EGF domain of PE(DELTAIa)-EGF(mutants) resulted in an increase in the binding affinity to EGF receptor and cytotoxicity to A431 cells. On the other hand, individual mutations of His16 to Asp and Gly18 to Ala in the EGF domain of PE(DELTAIa)-EGF(mutants) lead to a decrease in the binding affinity to EGF receptor and cytotoxicity to A431 cells. In addition, mutations of any of the cysteine residues of EGF in PE(DELTAIa)-EGF(mutants) resulted in the loss of their binding activity to EGF receptor and a corresponding loss of their cytotoxicity. This study indicates that the cytotoxicity of PE(DELTAIa)-EGF(mutant) to EGF receptor-bearing cells may be used as an indicator to screen mutations of EGF important in EGF-receptor interactions.

22/3,AB/15 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00679475
METHOD FOR PREPARING LIPOSOMES
VERFAHREN ZUR HERSTELLUNG VON LIPOSOMEN
PROCEDE DE PREPARATION DE LIPOSOMES
PATENT ASSIGNEE:
GENENTECH, INC., (210485), 460 Point San Bruno Boulevard, South Sa Francisco, CA 94080-4990, (US), (applicant designated states: D

INVENTOR:
*HSU, Chung, C."**, 13120 Delson Court, Los Altos Hills, CA 94022, (US
LEGAL REPRESENTATIVE:
Kiddle, Simon John et al (79861), Mewburn Ellis, York House, 23 Kingsway, London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 706374 A1 960417 (Basic)
EP 706374 B1 971210
WO 9501164 950112
APPLICATION (CC, No, Date): EP 95904347 940629; WO 94US7327 940629
PRIORITY (CC, No, Date): US 84933 930630
DESIGNATED STATES (Pub A): AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; (Pub B): DE; FR; GB
INTERNATIONAL PATENT CLASS: A61K-009/127;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9712W1	296
CLAIMS B	(German)	9712W1	293
CLAIMS B	(French)	9712W1	339
SPEC B	(English)	9712W1	8754
Total word count - document A			0
Total word count - document B			9682
Total word count - documents A + B			9682

22/3,AB/16 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0253440 DBA Accession No.: 2000-07930
Development of DNA delivery system using *Pseudomonas"** sp. *exotoxin"** *A"** and a DNA binding region of human DNA topoisomerase-I - a potential technique for cancer gene therapy
AUTHOR: Chen T Y; *Hsu C T"**; Chang K H; *Ting C Y"**; Whang-Peng J; Hui C E; +*Hwang J"**
CORPORATE AFFILIATE: Univ.Yang-Ming-Nat.Inst.Genet. Chinese-Acad.Sci.Inst.Zoology-Tapei Inst.Mol.Biol.Tapei
CORPORATE SOURCE: Institute of Molecular Biology, Academia Sinica, Nankang, Taipei, Taiwan, People's Republic of China.
JOURNAL: Appl.Microbiol.Biotechnol. (53, 5, 558-67) 2000
ISSN: 0175-7598 CODEN: EJABDD
LANGUAGE: English
ABSTRACT: Receptor-mediated gene delivery can offer high efficiency in gene transfer, but several technical difficulties need to be solved. The DNA binding regions of the human DNA topoisomerase (EC-5.99.1.2)-I (T1) to plasmid DNA were examined. Four DNA binding regions in human DNA T1 were identified. They resided in amino acids 51-200, 271-375, 422-596 and 651-696 of the human T1. One of the four regions was then used as a DNA binding *protein"** fragment in the construction of a DNA delivery vehicle. Based on the known functional property of each *Pseudomonas"** *exotoxin"** *A"** (PE) domain and human DNA T1, the receptor bi[redacted] and membrane translocation domains of PE were fused with a h positively charged DNA binding region of the N-terminal 198 amino residues of human DNA T1. The resulting recombinant *protein"* examined for DNA binding in vitro and transfer efficiency in cul cells. The results showed that this DNA delivery *protein"**

general DNA delivery vehicle without DNA sequence, topology, and cell-specificity. The DNA delivery *protein"** could be used to target genes of interest into cells for genetic and biochemical studies. (43 ref)

22/3,AB/17 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0087076 DBA Accession No.: 89-05067
Structure and function relationship of *Pseudomonas"** *exotoxin"** *A"**: an immunochemical study - characterization using antibody, potential application in vaccine production
AUTHOR: *Hwang J"**; Mei-shya Chen
CORPORATE SOURCE: Institute of Molecular Biology, Academia Sinica, Nankang, Taipei, Republic of China.
JOURNAL: J.Biol.Chem. (264, 4, 2379-84) 1989
CODEN: JBCHA3
LANGUAGE: English
ABSTRACT: Antisera were raised against *Pseudomonas"** *exotoxin"** *A"** (PE) and domains Ia and III to study the structure-function relationships of PE. Anti-PE antibody (AbPE) abolished ADP-ribosylation activity of PE. Neither antidomain Ia antibody nor antidomain III antibody inhibited the ADP-ribosylation activity of PE. This suggested that the inhibition of ADP-ribosylation by AbPE resulted from binding of AbPE to the region between domains Ia and III. Since binding of AbPE to PE did not inhibit NAD hydrolysis in the absence of elongation factor 2, the inhibitory effect of AbPE on ADP-ribosylation may be due to steric hindrance. The interface between domain Ia and III may be the site of entry of elongation factor 2. The antibodies were used to study the inhibitory effects of PE on *protein"** synthesis and its cytotoxic activity. AbPE or antidomain antibody reversed inhibition of *protein"** synthesis by PE and blocked its cytotoxicity. Rabbits immunized with domain Ia acquired tolerance to 100 ug of PE injected s.c. The results suggest that domain Ia may be used for vaccination against PE-mediated diseases. (22 ref)

22/3,AB/18 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0065095 DBA Accession No.: 87-09443
Functional domains of Pseudomonas exotoxin identified by deletion analysis of the gene expressed in E. coli - potentially useful for immunotoxin development
AUTHOR: *Hwang J"**; Fitzgerald D J; Adhya S; Pastan I
CORPORATE SOURCE: Laboratory of Molecular Biology, Division of Cancer Biology and Diagnosis, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.
JOURNAL: Cell (48, 1, 129-36) 1987
CODEN: CELLB5
LANGUAGE: English
ABSTRACT: Plasmids were constructed that expressed different portions of the 3-domain *exotoxin"** *A"** of *Pseudomonas"** aeruginosa (PE). PE gene was expressed in Escherichia coli using an inducible promoter. Results suggest that the binding activity and c

recognition function is located within the structural domain 1a. The structural domain 11 is required to translocate the toxin across a cellular membrane, and the structural domain 111 and a portion of domain 1b are required for *protein"** synthesis inhibition by ADP ribosylation activity. Toxin lacking domain 1a is about 100-fold less toxic to mice than intact PE and should be a useful molecule for the construction of immunotoxins. (28 ref)

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